with 3 molar equivalents of benzyl bromide, followed by 2.2 molar equivalents of sodium hydride. Upon completion, the reaction is quenched by addition of methanol, and the reaction mixture is concentrated, dissolved in one of the group consisting of ether, ethyl acetate, chloroform, or methylene chloride, and extracted with saturated aqueous sodium bicarbonate solution, then with brine. The organic layer is dried over either Na2SO4 or MgSO4, filtered, and concentrated. The residue is purified by chromatography on silica gel with a solvent system from the group consisting of ethyl acetate/hexanes, acetone/toluene, and methanol/chloroform. The product is dissolved in a solvent from the group consisting of DMF and DMSO at a concentration of 0.1 M and treated with 3 molar equivalents of benzyl alcohol, followed by 3 molar equivalents of sodium hydride. Upon completion, the reaction is cooled to 0%C, neutralized with acetic acid, and the reaction mixture is concentrated, dissolved in one of the group consisting of ether, ethyl acetate, chloroform, or methylene chloride, and extracted with saturated aqueous sodium bicarbonate solution, then with brine. The organic layer is dried over either Na2SO4 or MgSO4, filtered, and concentrated. The residue is purified by chromatography on silica gel with a solvent system from the group consisting of ethyl acetate/hexanes, acetone/toluene, and methanol/chloroform. The product is dissolved in CH2Cl2 to a concentration of 0.1M and 1 molar equivalent of triphenylphosphine is added. Upon completion, the reaction is concentrated and the residue treated with a 1:1 mixture of THF/water. Upon completion, the reaction mixture is concentrated, dissolved in one of the group consisting of ether, ethyl acetate, chloroform, or methylene chloride, and extracted with saturated aqueous sodium bicarbonate solution, then with brine. The organic layer is dried over either

Na2SO4 or MgSO4, filtered, and concentrated. The residue is purified by chromatography on silica gel with a solvent system from the group consisting of ethyl acetate/hexanes, acetone/toluene, and methanol/chloroform. This product is dissolved in DMF to a concentration of 0.1 M. 1.5 molar equivalents of Na2CO3 are added, followed by 1.1 equivalents of FmocCl. Upon completion, the reaction mixture is concentrated, dissolved in one of the group consisting of ether, ethyl acetate, chloroform, or methylene chloride, and extracted with saturated aqueous sodium bicarbonate solution, then with brine. The organic layer is dried over either Na2SO4 or MgSO4, filtered, and concentrated. The residue is purified by chromatography on silica gel with a solvent system from the group consisting of ethyl acetate/hexanes, acetone/toluene, and methanol/chloroform to give compound **54**.

Synthesis of compound 55 as illustrated in Figure 24. The alcohol component, selected from the group consisting of **40-46** (1 eq.), and the glycosyldonor, selcted from the group consisting of **34-39** (1.1 eq.) are dissolved in ether to a concentration of 0.1 M and treated at -30%C with *N*-iodosuccinimide (1.1 eq.) and 0.05 equivalents triflic acid. The reaction is then allowed to warm to ambient temperature. Upon completion, the reaction mixture is quenched by addition of saturated sodiumbicarbonate solution, concentrated, dissolved in one of the group consisting of ether, ethyl acetate, chloroform, or methylene chloride, and extracted with saturated aqueous sodium bicarbonate solution, then with brine. The organic layer is dried over either Na2SO4 or MgSO4, filtered, and concentrated. The residue is purified by chromatography on silica gel with a solvent system from the group consisting of ethyl acetate/hexanes, acetone/toluene, and methanol/chloroform. This product is dissolved in MeOH

to a concentration of 0.1 M and treated with lithium hydroxide (3 eq.) Upon completion of ester cleavage, the reaction mixture is quenched by addition of saturated ammonium chloride solution, concentrated, dissolved in one of the group consisting of ether, ethyl acetate, chloroform, or methylene chloride, and extracted with saturated aqueous sodium bicarbonate solution, then with brine. The organic layer is dried over either Na2SO4 or MgSO4, filtered, and concentrated. The residue is purified by chromatography on silica gel with a solvent system from the group consisting of ethyl acetate/hexanes, acetone/toluene, and methanol/chloroform.

A solution of this carboxylic acid at a concentration 0.2 M in DMF is treated with 1.1 eq. of an amine component, selected fro the group consisting of **24-28e**, HOBt (2eq.) and DIEA (1.1 eq). Then, HBTU (1.05 eq) is added in one portion. Upon completion, the solvent is removed and the reaction mixture is taken up in ethyl acetate and extracted twice with 1 N $NaHCO_3$. The organic layer is then dried over $MgSO_4$ and chromatographed over silica gel using a solvent system chosen from the group of ethyl acetate / hexane, toluene / acetone and chloroform / methanol.

This coupling product is dissolved in $MeOH/H_2O/AcOH$ (1:1:1) to a concentration of 0.1 M and treated with Pd/C 10% (1 wt. equivalent). The reaction is then hydrogenated over 40 psi of hydrogen until completion. The solvent is then removed and the residue is applied to a column of Amberlite CG-50 resin (NH_4 form) and eluted with a linear gradient of ammonia (0-5% conc. NH_3 in H_2O). Lyophilization of the appropriate fractions yields compound **55**.

Synthesis of compound 56 as illustrated in Figure 25: The

alcohol component, selected from the group consisting of **47-54** (1 eq.), and the glycosyldonor, selcted from the group consisting of **34-39** (1.1 eq.) are dissolved in ether to a concentration of 0.1 M and treated at -30%C with *N*-iodosuccinimide (1.1 eq.) and 0.05 equivalents triflic acid. The reaction is then allowed to warm to ambient temperature. Upon completion, the reaction mixture is quenched by addition of saturated sodiumbicarbonate solution, concentrated, dissolved in one of the group consisting of ether, ethyl acetate, chloroform, or methylene chloride, and extracted with saturated aqueous sodium bicarbonate solution, then with brine. The organic layer is dried over either Na2SO4 or MgSO4, filtered, and concentrated. The residue is purified by chromatography on silica gel with a solvent system from the group consisting of ethyl acetate/hexanes, acetone/toluene, and methanol/chloroform.

This product is dissolved in DMF to a concentration of 0.2 M and treated with an equal volume of piperidine. Upon completion of Fmoc-cleavage, the reaction mixture is quenched by addition of saturated ammonium chloride solution, concentrated, dissolved in one of the group consisting of ether, ethyl acetate, chloroform, or methylene chloride, and extracted with saturated aqueous sodium bicarbonate solution, then with brine. The organic layer is dried over either Na2SO4 or MgSO4, filtered, and concentrated. The residue is purified by chromatography on silica gel with a solvent system from the group consisting of ethyl acetate/hexanes, acetone/toluene, and methanol/chloroform.

A solution of this amine at a concentration 0.2 M in DMF is treated with 1.1 eq. of a carboxylic acid component, selected fro the group consisting of **24-28d**, HOBt (2eq.) and DIEA

(1.1 eq). Then, HBTU (1.05 eq) is added in one portion. Upon completion, the solvent is removed and the mixture is dissolved in ethyl acetate and extracted twice with 1 N $NaHCO_3$. The organic layer is then dried over $MgSO_4$ and chromatographed over silica gel using a solvent system chosen from the group of ethyl acetate / hexane, toluene / acetone and chloroform / methanol.

This coupling product is dissolved in a mixture of $MeOH/H_2O/AcOH$ (1:1:1) to a concentration of 0.1 M and treated with Pd/C 10% (1 wt. equivalent). The reaction is then hydrogenated over 40 psi of hydrogen until completion. The solvent is then removed and the residue is applied to a column of Amberlite CG-50 resin (NH_4 form) and eluted with a linear gradient of ammonia (0-5% conc. NH_3 in H_2O). Lyophilization of the appropriate fractions yields compound **56**.

Plasmon resonance and antimicrobial testing for Example 4. Synthesis of the biotinylated RNA and surface plasmon resonance detected binding experiments were performed as described vida supra. Solution conditions: 150 mM NaCl, 10 mM HEPES (pH 7.4), 3.4 mM EDTA. KD determination from the binding curves.

The fitting routine of the program kaleidagraph was used for all calculations. The starting values for a and b were set to 1 and 0 respectively. The number of KD values used in the fitting was adjusted depending on the observed range of equivalents bound but generally varied from 3 to 4.

Anti microbial testing: Kirby-Bauer disc test. These tests were performed exactly as described. Reference strains E. coli ATCC 25922, S. aureus ATCC 25923, and Ps. aeruginosa ATCC 27853 were obtained as packs of lyophilized

pellets (Difco), which were freshly reconstituted every few days. To make the antibiotic discs, paper discs (6mm diameter, BBL Microbiology Systems) were wetted through with 20mL of solution containing an appropriate amount (usually 33nmol) of antibiotic. The wet discs were placed in a dessicator overnight, and used the next day.

Minimal Inhibitory Concentration (MIC) testing. E. coli ATCC 25922 was grown in Mueller-Hinton broth (cation-adjusted, BBL Microbiology Systems) to an optical density of approx. 0.5 (absorbance read at 600nm), then diluted to an OD600 of 0.1. Samples of antibiotic were prepared in Mueller-Hinton broth, typically a series of 2-fold dilutions from 0.1mM to <1mM. 50mL of the diluted culture was added to 1 mL of each of the antibiotic samples, and the cultures were allowed to grow at 37°C for 4-6 hours, at which point the negative control sample (no antibiotic) typically had an absorbance of 1.2-1.5. The absorbance of each sample was read (l = 600nm), and MIC was considered to be the lowest antibiotic concentration at which the absorbance was less than 1% of the no-antibiotic control.

Synthesis of 5-O-benzyl-1,2-O-isopropylidene-α-D-xylofuranose (1300) as illustrated in Figure 27 . 1,2-O-isopropylidene-a-D-xylofuranose (1200) (4.2 g, 22.08 mmol; Aldrich/ common acetonide) was dissolved in toluene (120 mL) and treated with Bu_2SnO (5.76 g, 23.19 mmol). The reaction was then refluxed overnight with azeotropic removal of water. The Dean-Stark trap was then removed and replaced with a standard reflux condenser. The reaction was treated with BnBr (5.66 g, 33.12 mmol) and kept at 110 °C for 7 h. Upon addition of EtOAc and water, a solid formed which was filtered. The organic phase was washed with saturated sodium bicarbonate solution and brine and dried over Na2SO4. Chromatography of the resulting

oil using a gradient of 25% to 30% to 35% EtOAc in hexane afforded 4.01 g, 65% of the title compound as an oil which solidified after standing under vacuum. H1 NMR (CDCl3, 500 MHz): d1.31(s, 3H, acetonide methyl) , d1.48 (s, 3H, acetonide methyl), d3.68 (s,1H, OH), d3.90 (dd, 2H, J1=11Hz, J2= 4Hz, H5a), d3.93 (dd, 2H, J1=11Hz, J2= 4Hz, H5b), d4.25 (dd, 1H, J1=7Hz, J2= 4Hz, H4), d4.27 (m, 1H, H3), d4.50 (d, 1H, J=4Hz, H2), d4.60 (ABq, 2H, J=12Hz, Dn=29.7Hz, PhCH2O), d5.97, (d, 1H, J=4Hz, H1), d7.25-7.4 (m, 5H, C6H5); 13C NMR (CDCl3, 125 MHz): d 26.1, 26.7, 68.1, 74.0, 76.3, 78.0, 85.2, 104.8, 111.5, 127.8, 128.0, 128.5, 137.0; HRMS for C15H20O5 (M+Na): calcd. 303.1208; found 303.1201.

Synthesis of 5-O-benzyl-3-keto-1,2-O-isopropylidene-a-D-xylofuranose (1400) as illustrated in Figure 27. Methylene chloride (100mL) was cooled to -78 °C and DMSO (2.79g, 35.76 mmol) was added, followed by oxalyl chloride (2.18g, 17.16 mmol). The reaction was allowed to stir for 20 min at this temperature and then treated with a solution of 1300 (4.01g, 14.3 mmol) in 30 mL of CH2Cl2. The reaction was allowed to slowly warm to -35 °C and was kept at that temperature for 15 min before the addition of triethyl amine (7.24g, 71.5 mmol). The reaction was allowed to warm to room temperature and extracted with saturated sodium bicarbonate solution and saturated NaCl solution and dried over Na2SO4. Flash chromatography on 200 ml of silica gel using a gradient of 0 to 0.5 to 1 to 1.5% MeOH in CHCl3 afforded 3.2 g, 80.4 % of the title compound. H1 NMR (CDCl3, 500 MHz): d1.43 (s, 3H, acetonide methyl) , d1.46 (s, 3H, acetonide methyl), d3.72-3.75 (m, 2H, H5a and H5b), d4.35 (dd, J1=4 Hz, J2= 1 Hz, 1H, H2), d4.45 (m, 1H, H4), d4.51 (ABq, J=12 Hz, Dn=15.75 Hz, PhCH2O), d6.13 (d, J=4 Hz, H1), d7.2-7.4 (m, 5H, C6H5); 13C NMR (125 MHz): d 27.2, 27.6, 70.0, 73.6, 76.7, 79.8, 103.5,

114.1, 127.4, 127.8, 128.4, 128.5, 137.3; HRMS for C15H18O5 (M+Na): calcd. 301.1052; found 303.1043.

Synthesis of 5-O-benzyl-1,2-O-isopropylidene-a-D-ribofuranose (1500) as illustrated in Figure 27. Compound 1400 (3.2 g, 11.5 mmol) was dissolved in 50 ml of anhydrous methanol and treated with NaBH4 (218 mg, 5.75 mmol). The reaction was allowed to stir for one hour and then quenched with water. The solvent was removed and the reaction was partitioned between EtOAc and saturated sodium bicarbonate solution. The organic phase was dried with brine and Na2SO4. Flash chromatography on 120 ml of silica gel using a gradient of 25% to 3050 to 35% to 40% EtOAc in hexane afforded 2.53 g, 79% of the title compound. H1 NMR (CDC13, 500 MHz): d1.37 (s, 3H, acetonide methyl) , d1.56 (s, 3H, acetonide methyl), d2.42 (d, 1H, J=10 Hz, OH), d3.64 (dd, 1H, J1=11 Hz, J2= 4.5 Hz, H5a), d3.79 (dd, 1H, J1=11Hz, J2= 2.5 Hz, H5b), d3.92 (m, 1H, H4), d3.3.97 (m, 1H, H3), d4.56 (dd, 1H, J1=4.5Hz, J2= 3.5 Hz, 1H, H2), d4.60 (s, 2H, PhCH2O), d5.84 (d, 1H, J=3.5Hz, H1), d7.27-7.37 (m, 4H, C6H5); 13C NMR (CDC13, 125 MHz): d 26.4, 26.5, 68.5, 71.7, 73.5, 78.3, 79.7, 104.1, 112.6, 127.6, 127.7, 128.4, 137.8; HRMS for C15H20O5 (M+Na): calcd. 303.1208; found 303.1200.

Synthesis of 3-O-allyl-5-O-benzyl-1,2-O-isopropylidine-a-D-ribofuranose (1600) as illustrated in Figure 27. Compound 1500 (500 mg, 1.784 mmol) was dissolved in 10 ml of DMF and cooled to ice bath temperature. The reaction was treated with sodium hydride (47mg, 1.963 mmol) followed by allyl bromide (647 mg, 5.352 mmol). After 20 min, another 20 mg of NaH was added. After all starting material was consumed, the reaction was quenched with AcOH and the solvent was removed. The residue was taken up in EtOAc and washed with water,

saturated sodium bicarbonate solution, brine and dried over Na_2SO_4. Flash chromatography on 70 ml of silica gel using a gradient of 12% to 15% to 18% to 20% EtOAc in hexane afforded 555 mg, 97% of the title compound. H1 NMR ($CDCl_3$, 500 MHz): d1.36 (s, 3H, acetonide methyl) , d1.58 (s, 3H, acetonide methyl), d3.61 (dd, 1H, J1=11 Hz, J2= 4 Hz, H5a), d3.79 (dd, 1H, J1=11 Hz, J2= 2 Hz, H5b), d3.85 (dd, 1H, J1=9 Hz, J2= 4.5 Hz, H3), d4.07 (dddd, 1H, J1=12.5 Hz, J2= 6 Hz, J3= J4= 1.5 Hz, 1H, H4), d4.12-4.17 (m, 2H, CH_2CHCH_2O), d4.60 (ABq, 2H, J=12 Hz, Dn=45 Hz, $PhCH_2O$), d4.60 (dd, 1H, J1= J2= 4 Hz, H2), d5.21 (ddd, 1H, J1=11.5 Hz, J2= J3= 1.5 Hz, CH_2CHCH_2O), d5.28 (ddd, 1H, J1=17.5 Hz, J2= J3= 1.5 Hz, CH_2CHCH_2O), d5.78 (d, 1H, J=4 Hz, H1), d5.36-5.46 (m, 1H, CH_2CHCH_2O), d5.27-7.36 (m, 5H, C_6H_5); 13C NMR ($CDCl_3$, 125 MHz): d 26.4, 26.7, 67.8, 71.6, 73.5, 77.3, 77.4, 77.8, 103.9, 112.8, 118.0, 127.6, 127.7, 128.3, 134.4, 138.0; HRMS for $C_{18}H_{24}O_5$ (M+Na): calcd. 343.1521; found 343.1513.

Synthesis of 1,2-O-(4-nitrobenzoyl)-3-O-allyl-5-O-benzyl-a/b-D-ribofuranose (1100) as illustrated in Figure 27. Compound 1600 (757 mg, 2.36 mmol) was dissolved in 15 ml of dioxane and treated with 5 mL of 1N HCl solution. The reaction was then warmed to 80 °C for 1.5 h and cooled back to RT. The acid was quenched by addition of solid sodium bicarbonate and the solvent was removed. The residue was partitioned between water and EtOAc. The water layer was further extracted twice with EtOAc and the combined organic extracts were dried over $MgSO_4$. The solvent was removed and the residue was treated with pyridine (15 mL), 4-nitrobenzoyl chloride (1.04 g, 5.60) and a few crystals of DMAP. The reaction was stirred overnight and the solvent was removed. The residue was taken up in EtOAc and washed with water, saturated $CuSO_4$ solution followed by saturated ammonium chloride solution and brine.

The combined organic phases were dried over MgSO4 and the solvent was removed. The residue was chromatographed over 50 mL of silica gel using 10% to 12% to 15 % EtOAc in hexane to afford 910 mg, 68% (over 2 steps) of the product as a chromatographically separable mixture (approx. 4:1) of anomers. β anomer : H1 NMR (CDCl3, 500 MHz): d3.73 (dd, 1H, J1=11 Hz, J2=3 Hz, H5a), d3.86 (dd, 1H, J1=11 Hz, J2=2.5 Hz, H5b), d4.05-4.18 (m, 2H, CH2CHCH2O), d4.40 (ddd, 1H, J1=8 Hz, J2=J3= 3 Hz, H4), d4.53 (s, 2H, PhCH2O), d4.63 (dd, 1H, J1=8 Hz, J2=4.5 Hz, H3), d5.15-5.28 (m, 2H, CH2CHCH2O), d5.70 (d, 1H, J= 4.5 Hz, H2), d5.75-5.86 (m, 1H, CH2CHCH2O), d6.56 (s, 1H, H1), d7.20-7.30 (m, 5H, C6H5), d8.00-8.35 (m, 8H, C6H4NO2); 13C NMR (CDCl3, 125 MHz): d 68.5, 72.3, 73.5, 75.0, 75.8, 82.1, 99.4, 118.1, 123.5, 123.7, 127.6, 127.8, 128.4, 130.9, 131.0, 133.6, 134.5, 137.7, 150.6, 150.8, 163.0 163.5; HRMS for C29H26N2O11 (M+Na): calcd. 601.1434; found 601.1447; á anomer: H1 NMR (CDCl3, 500 MHz): d3.70 (dd, 2H, J1=3.5 Hz, J2=3 Hz, 2H, H5a&b), d4.05-4.10 (m, 2H, CH2CHCH2O), d3.70 (dd, J1=6.5 Hz, J2=3 Hz, 1H, H3), d4.55-4.60 (m, 3H, H4 and PhCH2O), d5.22-5.37 (m, 2H, CH2CHCH2O), d5.47 (dd, J1=6 Hz, J2=4 Hz, 1H, H2), d5.77-5.86 (m, 1H, CH2CHCH2O), d6.81 (d, J=4 Hz), d7.35-7.42 (m, 5H, C6H5), d8.08-8.30 (m, 8H, C6H4NO2); 13C NMR (CDCl3, 125 MHz): d 69,3, 72.1, 73.3, 73.7, 75.6, 84.9, 95.9, 117.3, 123.6, 127.7, 127.9, 128.5, 130.7, 131.0, 134.0, 134.4, 135.1, 137.5, 150.7, 163.5, 163.6; MS for C29H26N2O11 (M+Na): calcd. 601; found 601, for C29H26N2O11 (M+Cl-) calcd. 613; found 613.

Synthesis of 6,3',4'-tri-O-acetyl-3''-O-allyl, 5''-O-benzyl-1,3,2',6'-tetraazido ribostamycin (1800) as illustrated in Figure 28. Compound 1100 (3.5 g, 6.18 mmol) and compound 1000 (1.34 g, 2.43 mmol) were dissolved in 15 mL of CH2Cl2 and cooled in an ice bath. Then, BF3.OEt2 (922 mg, 6.5 mmol), was

added via syringe and the reaction was allowed to stir for 4.5 h. By this time a large amount of precipitate had formed. The reaction was quenched by addition of triethylamine until the solution became homogenous. Chloroform was added and the reaction was extracted with saturated NaHCO3 solution and brine and dried over Na2SO4. Chromatography over 200 mL of silica gel using a gradient of 5% to 10% to 15% to 20% to 25% to 30 % EtOAc in Hexane yielded 2.02 g of the donor, 1.47 g of the β anomer (63%) and 0.43 g of the α anomer (18%). b anomer: H1 NMR (CDCl3, 500 MHz): d1.61 (ddd, 1H, J1=J2=J3=13 Hz, H2 eq), d2.05 (s, 3H, COCH3), d2.08 (s, 3H, COCH3), d2.14 (s, 3H, COCH3), d2.37 (ddd, 1H, J1=13 Hz, J2=J3=4.5 Hz, H2 ax), d3.10 (dd, 1H, J1=11 Hz, J2=3.5 Hz, H2'), d3.22 (dd, 1H, J1=13.5 Hz, J2=5.5 Hz, H6'a),d3.32 (dd, 1H, J1=13.5 Hz, J2=3 Hz, H6'b), d3.42 (ddd, 1H, J1=13 Hz, J2=10 Hz, J3=4.5 Hz, H1), d3.49 (ddd, 1H, J1=13 Hz, J2=10 Hz, J3=4.5 Hz, H3), d3.58 (dd, 1H, J1=10.5 Hz, J2=4.5 Hz, H5''a), d3.68 (dd, 1H, J1=J2=10 Hz, H4), d3.82 (dd, 1H, J1=10.5 Hz, J2=2.5 Hz, H5''b), d3.85 (dd, 1H, J1=J2=10 Hz, H5), d3.90 (dd, 1H, J1=12.5 Hz, J2=6 Hz, CH2CHCH2O), d4.00 (dd, 1H, J1=12.5 Hz, J2=5.5 Hz, 1H, CH2CHCH2O), d4.16-4.22 (m, 2H, H3'' and H4''), d4.38-4.42 (m, 1H, H5'), d4.58 (ABq, 2H, J=11.5 Hz, Dn=51.2 Hz, PhCH2O), d4.86 (dd, 1H, J1=J2=10 Hz, H4'), d4.96 (dd, 1H, J1=J2=10 Hz, H6), d5.09 (dd, 1H, J1=10 Hz, J2=1.5 Hz, CH2CHCH2O), d5.16 (dd, J1=17 Hz, J2=1.5 Hz, 1H, CH2CHCH2O), d5.29 (d, 1H, J=3 Hz, H2''), d5.38 (dd, 1H, J1=11 Hz, J2=9.5 Hz, H3'), d5.40 (s, 1H, H1''), d5.63-5.74 (m, 1H, CH2CHCH2O), d6.07 (d, 1H, J=3.5 Hz, H1'), d7.2-7.35 (m, 5H, C6H5), d8.15-8.35 (m, C6H4NO2); 13C NMR (CDCl3, 125 MHz): d 20.7, 20.9, 31.3, 50.9, 58.1, 58.9, 61.0, 69.0, 69.2, 69.4, 70.2, 73.5, 75.1, 75.9, 76.2, 76.6, 80.4, 82.6, 96.1, 107.8, 118.1, 123.7, 127.8, 127.9, 128.6, 130.9, 133.5, 134.7, 137.7, 150.8, 163.5, 169.7, 170.0; HRMS for C40H45N13O16 (M+Na):

calcd. 986.3005; found 986.3035. a anomer: H1 NMR (CDCl3, 500 MHz): d1.58 (ddd, 1H, J1=J2=J3=13 Hz, H2 eq), d2.04 (s, 3H, COCH3), d2.10 (s, 3H, COCH3), d2.14 (s, 3H, COCH3), d2.38 (ddd, 1H, J1=13 Hz, J2=J3=4.5 Hz, H2 ax), d3.18 (dd, 1H, J1=13.5 Hz, J2=4.5 Hz, H6'a), d3.30-3.37 (m, 2H, H6'b, H2'), d3.43 (ddd, 1H, J1=12 Hz, J2=10 Hz, J3=4.5 Hz, H3), d3.50 (ddd, 1H, J1=12.5 Hz, J2=10 Hz, J3=4.5 Hz, H1), d3.57 (dd, 1H, J1=J2=9.5 Hz, H4), d3.58 (dd, 1H, J1=11 Hz, J2=4 Hz, H5'a), d3.71 (dd, 1H, J1=11 Hz, J2=2.5 Hz, H5'b), d3.80 (dd, 1H, J1=J2=9.5 Hz, H5), d3.88-4.02 (m, 2H, CH2CHCH2O), d4.08 (dd, J1=7.5 Hz, J2=5 Hz, 1H, H3''), d4.22-4.26 (m, 1H, H4''), d4.42-4.47 (m, 1H, H5'), d4.58 (ABq, 2H, J=12 Hz, Dn=43.5 Hz, PhCH2O), d4.92-4.99 (m, 2H, H6, H4'), d5.08-5.19 (m, 2H, CH2CHCH2O), d5. 47-5.44 (m, 2H, H1', H3'), d5.58 (d, 1H, J=4 Hz, H1''), d5.67 (dd, 1H, J1=J2=5 Hz, H2''), d5.67-5.76 (m, 1H, CH2CHCH2O), d7.28-7.42 (m, 5H, C6H5), d8.23-8.35 (m, 2H, C6H4NO2); 13C NMR (CDCl3, 125 MHz): d 20.57, 20.63, 21.1, 31.5, 50.5, 58.1, 58.6, 61.0, 68.7, 69.0, 69.4, 70.3, 71.5, 72.0, 73.5, 73.6, 75.8, 79.4, 80.0, 82.5, 97.4, 103.0, 118.1, 123.7, 127.8, 128.4, 130.4, 131.1, 133.6, 134.7, 137.6, 150.8, 164.2, 169.6, 169.9, 170.0; HRMS for C40H45N13O16 (M+Cs): calcd. 1096.2162; found 1096.2119.

Synthesis of 3''-O-allyl-5''-O-benzyl-1,3,2',6'-tetraazido ribostamycin (1900) as illustrated in Figure 28. Compound 1800 (1.47 g, 1.525 mmol) was dissolved in a mixture of MeOH and dioxane 1:1 (30 mL). The reaction was then treated with a solution of LiOH (384 mg, 9.151 mmol) in 10 mL of H2O. The mixture was allowed to stir overnight at room temperature and the solvent was removed. The reaction was partitioned between EtOAc and saturated NaHCO3 and extracted 3 times with EtOAc. The combined organic phases were dried over MgSO4 and purified on 100 mL of silica gel using 50% to 55% to 60%

EtOAc in hexane to afford 947 mg, 93 % of product as a white foam. 1H NMR (CD3OD, Bruker AMX-500): d1.35 (ddd, 1H, J1=J2=J3=12.5 Hz, H2 eq), d2.19 (ddd, J1=12.5 Hz, 1H, J2=J3=4.5 Hz, H2 ax), d3.02 (dd, 1H, J1=10.5 Hz, J2=4 Hz, H2'), d3.27 (dd, 1H, J1=10 Hz, J2=9 Hz, H4'), d3.34-3.45 (m, 3H, H1, H3, H6'a), d3.46-3.54 (m, 1H, H5),d3.50 (dd, 1H, J1=13 Hz, J2=2.5 Hz, H6'b), d3.58 (dd, 1H, J1=11 Hz, J2=5.5 Hz, H5''a), d3.61-3.65 (m, 2H, H4, H6), d3.72 (dd, 1H, J1=11 Hz, J2=3 Hz, H5''b), d3.84 (dd, 1H, J1=10.5 Hz, J2=9 Hz, H3'), d3.98 (dddd, 1H, J1=12.5 Hz, J2=6Hz, J3=J3=1.5 Hz, CH2CHCH2O), d4.01 (dd, 1H, J1=7 Hz, J2=4.5 Hz, H3''), d4.06-4.15 (m, 3H, H5', H4'', CH2CHCH2O), d4.31 (dd, 1H, J1=4.5 Hz, J2=1 Hz, H2''), d4.57 (ABq, 2H, J=12 Hz, Dn=25.3 Hz, PhCH2O), d5.15 (ddd, J1=10.5 Hz, J2=J3=1.5 Hz, 1H, CH2CHCH2O), d5.27 (ddd, 1H, J1=17 Hz, J2=J3=1.5 Hz, CH2CHCH2O), d5.33 (d, 1H, J=1 Hz, H1''), d5.86-5.94 (m, 1H, CH2CHCH2O), d5.91 (d, 1H, J=4 Hz, H1'), d7.25-7.40 (m, 5H, C6H5); 13C NMR (CD3OD, 125 MHz): d 33.1, 52.6, 61.3, 61.8, 64.8, 71.6, 72.3, 72.4, 72.6, 73.1, 74.3, 74.5, 77.2, 77.4, 79.1, 81.4, 85.4, 97.9, 110.6, 117.8, 128.7, 129.0, 129.4, 135.9, 139.4; HRMS for C27H36N12O10 (M+Cs): calcd. 821.1732; found 821.1726.

Synthesis of 3''-O-allyl-6,3',4',3'',5''-penta-O-benzyl-1,3,2',6'-tetraazido ribostamycin (900) as illustrated in Figure 28. Compound 1900 (974 mg, 1.414 mmol) was dissolved in 20 mL of DMF and treated with 8 mL of BnBr. The solution was cooled using an ice bath and treated with sodium hydride (204 mg, 8.484 mmol) in one portion. The cooling bath was then removed and the reaction was stirred for one hour. AcOH was added to quench the NaH and the solvent was removed. The reaction was picked up in EtOAc and washed with water twice. The organic phases were combined and dried over MgSO4 and purified on 100 mL of silica gel using 10% to 12.5% to 15%

EA/H to afford 1.24 g, 84% of product. 1H NMR (CDCl3, 500 MHz): d1.43 (ddd, 1H, J1=J2=J3=12.5 Hz, H2 eq), d2.26 (ddd, 1H, J1=12.5 Hz, J2=J3=4.5 Hz, H2 ax), d3.20-3.27 (m, 2H, H5, H2'), d3.30 (dd, 1H, J1=13.5 Hz, J2=5 Hz, H6'a), d3.35-3.45 (m, 3H, H1, H3, H4'), d3.30 (dd, 1H, J1=13.5 Hz, J2=2.5 Hz, H6'b), d3.58 (dd, 1H, J1=10.5 Hz, J2=4.5 Hz, H5''a), d3.60-3.72 (m, 3H, H4, H6, H5''b), d3.72-3.82 (m, 2H, CH2CHCH2O), d3.84 (dd, 1H, J1=J2=5.5 Hz, H3''), d3.92 (dd, 1H, J1=5 Hz, J2=3.5 Hz, H2''), d3.98 (dd, 1H, J1=10 Hz, J2=9 Hz, H3'), d4.15-4.22 (m, 2H, H4'', H5'), d4.42-4.90 (m, 10 H, PhCH2O), d5.12 (ddd, J1=10.5 Hz, J2=J3=1.5 Hz, 1H, CH2CHCH2O), d5.12 (ddd, J1=17 Hz, J2=J3=1.5 Hz, 1H, CH2CHCH2O), d5.12 (d, 1H, J=3Hz, H1''), d5.75-5.84 (m, 1H, CH2CHCH2O), d5.96 (d, 1H, J=3.5Hz, H1'), d7.2-7.4 (m, 25 H, C6H5); 13C NMR (CDCl3, 125 MHz): d 32.2, 51.1, 59.6, 60.4, 63.5, 70.2, 70.9, 71.0, 72.3, 73.3, 74.9, 75.1, 75.5, 76.1, 78.5, 80.1, 80.5, 80.8, 81.2, 83.3, 96.0, 107.3, 116.8, 127.5, 127.8, 127.9, 128.1, 128.3, 128.4, 134.5, 137.4, 137.8, 138.0, 138.2; HRMS for C55H60N12O10 (M+Cs): calcd. 1181.3610; found 1181.3641.

Synthesis of 6,3',4',3'',5''-penta-O-benzyl-1,3,2',6'-tetraazido ribostamycin (2000) as illustrated in Figure 28. Bis (methyldiphenylphoshino)cyclooctadienyl IrI hexafluorophosphate (40 mg, 0.05 mmol) was suspended in THF (5mL) and H2 was bubbled through this suspension for 20 minutes. The resulting clear solution was transferred via syringe into a solution of compound 9 (1.24 g., 1.18 mmol) in THF (15 mL). After 1 h., a quantitative conversion to a slightly less polar material was observed by TLC (25% EtOAc in hexane). The solvent was removed and the residue was co-rotary evaporated with CH2Cl2 several times. The reaction was then taken up in CH2Cl2 (30 mL) and treated with trimethylamine N-oxide dihydrate (197 mg, 1.77 mmol), and a

solution of OsO_4 in tBuOH (enough solution to deliver 3 mg of OsO_4 , 0.012 mmol). After the reaction was complete (overnight) the solvent was removed and the residue was purified over 100 mL of silica gel using 20% to 25% to 30% EtOAc in hexane to obtain 1.11 g, 93.3% of the title compound as a colorless oil. 1H NMR ($CDCl_3$, 500 MHz): d1.45 (ddd, 1H, J1=J2=J3=12.5 Hz, H2 eq), d2.28 (ddd, J1=12.5 Hz, 1H, J2=J3=4.5 Hz, H2 ax), d2.35 (d, 1H, J=4 Hz, OH), d3.21 (dd, 1H, J1=10.5 Hz, J2=4 Hz, H2'), d3.25 (dd, 1H, J1=J2=9 Hz, H5), d3.21 (dd, 1H, J1=13 Hz, J2=5 Hz, H6'a), d3.35-3.44 (m, 3H, H1, H3, H4'), d3.47 (dd, 1H, J1=13 Hz, J2=2.5 Hz, H6'b), d3.57 (dd, 1H, J1=10.5 Hz, J2=4 Hz, H5''a), d3.61 (dd, 1H, J1=J2=9 Hz, H4 or H6), d3.65 (dd, 1H, J1=J2=9 Hz, H4 or H6), d3.72 (dd, 1H, J1=10.5 Hz, J2=3 Hz, H5'b), d3.92 (dd, 1H, J1=4 Hz, J2=3 Hz, H2''), d3.97 (dd, 1H, J1=10.5 Hz, J2=4 Hz, H3'), d4.00-4.06 (m, 2H, H3'', H4''), d4.15-4.20 (m, 1H, H5'), d4.39 (ABq 2H, J= 11.5, Dn= 23.6 Hz, $PhCH_2O$), d4.52 (d, 1H, J=12.5 Hz, $PhCH_2O$), d4.60 (dd, 2H, J1=J2=11 Hz, $PhCH_2O$), d4.76 (d, 1H, J=11 Hz, $PhCH_2O$), d4.80-4.90 (m, 4H $PhCH_2O$), d5.45 (d, 1H, J=3 Hz, H1''), d5.98 (d, 1H, J=4 Hz, H1'), d7.13-7.40 (m, 25H, C_6H_5); 13C NMR ($CDCl_3$, 125 MHz): d 32.3, 51.1, 59.6, 60.6, 63.5, 70.5, 70.6, 70.9, 72.9, 73.3, 74.9, 75.37, 75.41, 76.0, 78.5, 80.1, 81.6, 82.2, 83.0, 83.5, 127.5, 127.6, 127.8, 128.0, 128.1, 128.4, 128.5, 137.1, 137.4, 137.76, 137.78, 138.1; HRMS for $C_{52}H_{56}N_{12}O_{10}$ (M+Cs): calcd. 1141.3297; found 1141.3267.

Synthesis of 3''-O-(ethan-2-alo)-6,3',4',3'',5''-penta-O-benzyl-1,3,2',6'-tetraazido ribostamycin (2100) as illustrated in Figure 29. Compound 900 (112 mg, 107 mmol) was dissolved in CH_2Cl_2 (5mL) and cooled to -78 °C. Ozone was passed through the solution until the blue color persisted. Then DMS (66mL, 1.07 mmol) was added to the reaction and the

mixture was stirred at ambient temperature for 2 days. The solvent was removed and the residue was chromatographed over 50 mL of silica gel using a 25% to 30% to 35% to 40% gradient of EtOAc in hexane to afford 83 mg, 74% of the title compound as an oil. 1H NMR (CDCl3, 500 MHz): d1.44 (ddd, 1H, J1=J2=J3=12.5 Hz, H2 eq), d2.17 (ddd, 1H, J1=12.5 Hz, J2=J3=4.5 Hz, H2 ax), d3.19-3.25 (m, 2H, H5, H2'), d3.30 (dd, 1H, J1=11 Hz, J2=5 Hz, H6'a), d3.36-3.45 (m, 3H, H4', H1, H3), d3.48 (dd, 1H, J1=11 Hz, J2=2 Hz, H6'b), d3.59 (dd, 1H, J1=10 Hz, J2=4 Hz, H5''a), d3.62-3.78 (m, 5H, H4,H6, H5''b, OCH2CHO), d3.80 (dd, 1H, J1=J2=4.5 Hz, H3''), d3.92 (dd, 1H, J1=4.5 Hz, J2=3.5 Hz, H2''), d3.99 (dd, 1H, J1=9.5 Hz, J2=9 Hz, H3'), d4.15-4.22 (m, 2H, H4'', H5'), d4.46-4.90 (m, 10H, PhCH2O), d5.58 (d, 1H, J1=3.5 Hz, H1''), d5.93 (d, 1H, J1=3.5 Hz, H1'), d7.23-7.37 (m, 25H, C6H5); 13C NMR (CDCl3, 125 MHz): d 32.3, 51.1, 59.6, 60.4, 63.5, 69.9, 71.0, 72.7, 73.4, 74.9, 75.0, 75.2, 75.5, 76.0, 78.5, 78.9, 80.0, 80.7, 80.8, 81.0, 83.4, 96.0, 106.7, 127.4, 127.6, 127.7, 127.8, 127.9, 128.1, 128.4, 137.5, 137.6, 137.7, 138.0, 200.4; MS: for C54H58N12O11 (M+Cs): calcd. 1183; found 1183 (the peak was too weak for an exact match).

Synthesis of 3''-O-2-N-(3-N-Cbz-propylamino)-ethylamino-6,3',4',3'',5''-penta-O-benzyl-1,3,2',6'-tetraazido ribostamycin (2200) as illustrated in Figure 29. Compound 2100 (50 mg, 48 mmol) was suspended in MeOH (2mL) . A solution of mono-CBZ propylene diamine (81 mg, 389 mmol) was made up in MeOH (2 mL) and acidified with glacial acetic acid until pH 6 (pH paper). This solution was then added to the aldehyde mixture and to this was added THF until homogeneity was achieved. The reaction was treated with an excess of solid NaCNBH3 and the amination was complete in minutes. The reaction was diluted with ethyl acetate and extracted with 1

N NaOH twice. The organic phases were dried over MgSO4 and the solvent was removed. The residue was purified on 50 mL of silica gel using a gradient of 2% to 3% to 4% to 5% MeOH in CHCL3 to afford 32 mg, 54% of the title compound. 1H NMR (CDC13, 500 MHz): d1.42 (ddd, 1H, J1=J2=J3=12.5 Hz, H2 eq), d1.45-1.53 (m, 2H, NHZCH2CH2CH2NH-), d2.24 (ddd, 1H, J1=12.5 Hz, J2=J3=4.5 Hz, H2 ax), d2. 50-2.58 (m, 2H, NHZCH2CH2CH2NH-), d2.55-2.66 (m, 2H, N-CH2CH2-O), d3.09-3.22 (m, 2H, NHZCH2CH2CH2NH-), d3.18-3.31 (m, 4H, H5, H2', N-CH2CH2-O), d3.30 (dd, 1H, J1=13.5 Hz, J2=5.5 Hz, H6'a), d3.34-3.42 (m, 2H, H1, H3), d3.41 (dd, 1H, J1=J2=9.5 Hz, H4'), d3.48 (dd, 1H, J1=13.5 Hz, J2=2.5 Hz, H6'b), d3.56 (dd, 1H, J1=10.5 Hz, J2=4 Hz, H5''a), d3.59-3.69 (m, 3H, H4, H6, H5''b), d3.78 (dd, 1H, J1=J2=5 Hz, H3''), d3.93 (dd, 1H, J1=5 Hz, J2=3.5 Hz, H2''), d3.98 (dd, 1H, J1=J2=9.5 Hz, H3'), d4.12-4.21 (m, 2H, H5', H4''), d4.42-4.55 (m, 3H, PhCH2O), d4.56-4.63 (m, 2H, PhCH2O), d4.73-4.90 (m, 5H, PhCH2O), d5.05-5.10 (m, 2H, PhCH2O), d5.45-5.50 (m, 1H, NHZCH2CH2CH2NH-), d5.55 (d, 1H, J=3.5 Hz, H1''), d5.95 (d, 1H, J=3.5 Hz, H1'), d7.23-7.37 (m, 30 H, C6H5); 13C NMR (CDC13, 125 MHz): d 29.1, 29.7, 32.2, 39.9, 47.5, 49.1, 51.1, 59.6, 60.4, 63.5, 6.4, 69.1, 70.3, 70.9, 72.3, 73.3, 74.9, 75.0, 75.4, 76.2, 78.1, 78.5, 80.1, 80.4, 80.8, 81.1, 83.3, 96.0, 107.1, 127.5, 127.6, 127.7, 127.9, 128.1, 128.3, 128.4, 128.5, 136.8, 137.6, 137.60, 137.83, 138.1, 156.4; HRMS: for C65H74N14O12 (M+Cs): calcd. 1375.4665; found 1375.4709.

Synthesis of 3''-O-2-N-(3-propylamino)-ethylamino ribostamycin (600)as illustrated in Figure 29. Compound 2200 (45 mg, 36 mmol) was dissolved in THF (5mL) and treated with H20 (500 mL) and 1 N NaOH (50 mL). A solution of PMe3 in THF (159 mL of a 1 N solution) was added and the reaction was allowed to stir for 10 h. The reaction mixture was then

loaded onto a 50 mL column of silica gel and eluted with a gradient of 0% to 2.5% to 5% to 10% conc. NH3 in MeOH. The product fractions were pooled and coevaporated with THF (3 times). THF (7 mL) was added via syring to a dry 3 neck flask equipped with a Dewar condenser. Then ammonia (~20 mL) was condensed into the reaction vessel. A chunk of Na (93 mg, 4 mmol) was then allowed to dissolve in the ammonia for 15 min. Then a solution of the polyamine in a mixture of EtOH and THF (500 mL each) was added in one portion and washed down with THF. The reaction was stirred until the blue color was discharged. Then an aqueous solution of ammonium fomate (235 mg, 3.7 mmol) was added and the ammonia was allowed to evaporate overnight. The remaining solvent was removed in vacuo and the residue was loaded onto a column of Amberlite CG-50 cation exchange resin (0.5 cm x 7 cm) in its NH4+ form and eluted with a linear gradient of 0% to 7.5 % NH3 in H2O (100 mL of each in a gradient maker). After lyophilization, neutralization and relyophilization, 21.5 mg, 75% of 606 HCl salt was obtained. 1H NMR (D2O, pD 2 with Cl- as counterinon, 500 MHz): d1.95 (ddd, 1H, J1=J2=J3=12.6 Hz, H2 eq), d2.09-2.17 (m, 2H, NH2CH2CH2CH2NH-), d2.53 (ddd, 1H, J1=12.6 Hz, J2=J3=4.1 Hz, H2 ax), d3.13 (dd, 2H, J1=J2=7.9 Hz, NH2CH2CH2CH2NH-), d3.23 (dd, 2H, J1=J2=8.0 Hz, NH2CH2CH2CH2NH-), d3.33 (dd, 1H, J1=13.2 Hz, J2=6.4 Hz, H6'a), d3.32-3.39 (m, 2H, N-CH2CH2-O), d3.40 (ddd, 1H, J1=12.6 Hz, J2=10.6 Hz, J3=4.1 Hz, H1), d3.44-3.52 (m, 2H, H2', H6'b), d3.52 (dd, 1H, J1=J2=9.5 Hz, H4'), d3.60 (ddd, 1H, J1=12.6 Hz, J2=10.4 Hz, J3=4.1 Hz, H3), d3.72-3.78(m, 2H, H6, H5''a), d3.88-4.01 (m, 5H, N-CH2CH2-O, H5''b, H5', H5), d4.04 (dd, 1H, J1=10.9 Hz, J2=9.5 Hz, H3'), d4.11 (dd, 1H, J1=7.2 Hz, J2=4.6 Hz, H3''), d4.18 (dd, 1H, J1=10.4 Hz, J2=9.9 Hz, H4), d4.18-4.21 (m, 1H, H4''), d4.48 (dd, 1H, J1=4.6 Hz, J2=1.7 Hz, H2''), d5.45 (d, 1H, J=1.6 Hz, H1''),

d6.06 (d, 1H, J=3.9 Hz, H1'); 13C NMR (CDCl3, 500 MHz): d 25.1 (NH2CH2CH2CH2NH-), 29.5 (C2), 38.0 (NH2CH2CH2CH2NH-), 41.5 (C6'), 46.0 (NH2CH2CH2CH2NH-), 48.8 (N-CH2CH2-O), 49.9 (C3), 51.3 (C1), 55.0 (C2'), 62.3 (C5''), 66.5 (N-CH2CH2-O), 69.5 (C3'), 70.9 (C5'), 72.0 (C4'), 74.0 (C6), 76.9 (C4), 78.4 (C3''), 82.6 (C4''), 86.2 (C5), 97.1 (C1'), 112.0 (C1''); MS: for C22H46N6O10 (M+H): calcd. 555; found 555, for C23H45N5O14 (M-H): calcd. 553; found 553.

Synthesis of 3''-O-2-N-(paramethoxybenzyl, Cbz)-ethylamino-6,3',4',3'',5''-penta-O-benzyl-1,3,2',6'-tetraazido ribostamycin (2300)as illustrated in Figure 29. Compound 2100 (76 mg, 72 mmol) was suspended in MeOH (2mL) . A solution of para-methoxybenzylamine (99 mg, 720 mmol) was made up in MeOH (2 mL) and acidified with glacial acetic acid until pH 6 (pH paper). This solution was then added to the aldehyde mixture and to this was added THF until homogeneity was achieved. The reaction was treated with an excess of solid NaCNBH3 and the amination was over in a matter of minutes. The reaction was diluted with ethyl acetate and extracted with 1 N NaOH twice. The organic phases were dried over MgSO4 and the solvent was removed. The residue was purified on 50 mL of silica gel using a gradient of 2% to 3% to 4% to 5% MeOH in CHCL3. The resulting amine was then dissolved in CH2Cl2 and treated with ZOSu (22mg, 86 mmol). The reaction mixture was then directly chromatographed on 50 mL of silica gel using a gradient of 5% to 10% to 15% Ethyl Acetate in Hexane to afford 65 mg, 69% of the title compound. 1H NMR (CDCl3, 500 MHz): d1.43 (ddd, 1H, J1=J2=J3=12.5 Hz, H2 eq), d2.25 (ddd, 1H, J1=12.5 Hz, J2=J3=4.5 Hz, H2 ax), d3.22 (dd, 1H, J1=10.5 Hz, J2=4 Hz, H2'), d3.16-3.35 (m, 4H, N-CH2CH2-O), d3.30 (dd, 1H, J1=13.5 Hz, J2=5.5 Hz, H6'a), d3.30-3.44 (m, 3 H, H1, H3, H4'), d3.47 (dd, 1H, J1=13.5 Hz, J2=2.5 Hz,

H6'b), d3.45-3.55 (m, 1H, H5''a), d3.58-3.61 (m, 3H, H4, H6, H5''b), d3.62-3.71 (m, 4H, OMe, H3''), d3.83-3.93 (m, 1H, H2''), d3.97 (dd, 1H, J1=10.5 Hz, J2=9 Hz, H3'), d4.03-4.15 (m, 1H, H4''), d4.15-4.21 (m, 1H, H5'), d4.32-4.52 (m, 5H, PhCH2O), d4.59 (d, J=12 Hz, 2H, PhCH2O), d4.71-4.89 (m, 5H, PhCH2O), d5.14 (s, 2H, PhCH2O), d5. 48-5.52 (m, 1H, H1''), d5. 92-5.98 (m, 1H, H1'), d6.76 (dd, J1=17.5 Hz, J2=8 Hz, C6H4OMe), d7.04 (dd, J1=61 Hz, J2=8 Hz, 2H, C6H4OMe), d7.14-7.37 (m, 30 H, C6H5); 13C NMR (CDCl3, Bruker 125 MHz): d 32.2, 45.6, 46.5, 50.78, 50.82, 51.1, 55.2, 59.6, 60.5, 63.5, 67.2, 68.8, 70.2, 70.3, 70.9, 72.36, 72.39, 73.3, 74.9, 75.06, 75.10, 75.4, 76.11, 76.15, 78.3, 78.5, 80.1, 80.6, 80.78, 80.84, 81.2, 81.4, 83.3, 96.0, 107.4, 107.5, 113.8, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 128.7, 129.4, 129.8, 137.5, 137.8, 138.1; HRMS: for C70H75N13O13 (M+Cs): calcd. 1438.4662; found 1438.4597.

Synthesis of 3''-O-2-N-Cbz-ethylamino-6,3',4',3'',5''-penta-O-benzyl-1,3,2',6'-tetraazido ribostamycin (2400) as illustrated in Figure 29. Compound 2300 (65 mg, 50 mmol) was dissolved in a mixture of acetonitrile and water (9:1, 4 mL) and treated with CAN (136 mg, 249 mmol). After 4.5 h., the reaction was quenched by addition of a 1 N solution of Na2S2O4. The aqueous layer was extracted twice with ethyl acetate and the pooled organic phases were dried over MgSO4. Chromatography of the residue over 40 mL of silica gel using a gradient of 15% to 20% to 25% to 30% ethyl acetate in hexane afforded 49 mg, 83% of product. 1H NMR (CDCl3, 500 MHz): d1.42 (ddd, 1H, J1=J2=J3=12.5 Hz, H2 eq), d2.26 (ddd, 1H, J1=12.5 Hz, J2=J3=4.5 Hz, H2 ax), d3.05-3.27 (m, 6H, H5, H2', NHZCH2CH2-O), d3.31 (dd, 1H, J1=13.5 Hz, J2=5 Hz, H6'a), d3.34-3.43 (m, 2H, H1, H3), d3.42 (dd, 1H, J1=J2=9.5 Hz, H4'), d3.48 (dd, 1H, J1=13.5 Hz, J2=2.5 Hz, H6'b), d3.54 (dd,

1H, J1=10.5 Hz, J2=4 Hz, H5''a), d3.56-3.66 (m, 3H, H4, H6, H5''b), d3.71 (dd, 1H, J1=J2=5 Hz, H3''), d3.89 (dd, 1H, J1=5 Hz, J2=3 Hz, H2''), d3.97 (dd, J1=10 Hz, J2=9.5 Hz, 1H, H3'), d4.07-4.12 (m, 1H, H4''), d4.17-4.22 (m, 1H, H5'), d4.42-4.53 (m, 3H, PhCH2O), d4.59 (d, J=12 Hz, 2H, PhCH2O), d4.73-4.89 (m, 5H, PhCH2O), d5.06 (s, 2H, PhCH2O), d5.13-5.18 (m, 1H, NHZCH2CH2-O), d5.52 (d, 1H, J=3 Hz, H1''), d5.91 (d, 1H, J=3.5 Hz, H1'), d7.10-7.7.45 (m, 30H, C6H5); 13C NMR (CDCl3, 125 MHz): d 29.7, 32.3, 40.9, 51.1, 59.5, 60.4, 63.5, 66.6, 68.9, 70.2, 70.9, 72.4, 73.3, 74.9, 75.0, 75.5, 76.2, 78.3, 78.5, 80.1, 80.2, 80.7, 81.0, 83.3, 96.0, 107.1, 127.3, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 136.5, 137.5, 137.6, 137.7, 138.0, 156.3; HRMS: for C62H67N13O12 (M+Cs): calcd. 1318.4086; found 1318.4032.

Synthesis of 3''-O-Ethyl-2-amino ribostamycin (500) as illustrated in Figure 29. The deprotection was carried out starting with compound 2400 in the exact manner as the preparation of compound 600 to afford the title substance in 33% yield. It should be noted that this is a result from a single experiment where there was a problem with the reduction of the azides and a better yield can probably be obtained. 1H NMR (D2O, pD 2 adjusted with DCl, 500 MHz): d1.41 (ddd, 1H, J1=J2=J3=12.6 Hz, H2 eq), d2.24 (ddd, 1H, J1=12.6 Hz, J2=J3=4.1 Hz, H2 ax), d3.26 (dd, 2H, J1=J2=4.9 Hz, NH2CH2CH2-O), d3.32 (dd, 1H, J1=13.6 Hz, J2=6.4 Hz, H6'a), d3.41 (ddd, 1H, J1=12.6 Hz, J2=10.7 Hz, J3=4.1 Hz, H1), d3.44-3.52 (m, 2H, H2', H6'b), d3.51 (dd, 1H, J1=J2=9.3 Hz, H4'), d3.60 (ddd, 1H, J1=12.6 Hz, J2=10.5 Hz, J3=4.1 Hz, H3), d3.71-3.78 (m, 2H, H5''a, H6), d3.83-3.92 (m, 2H, NH2CH2CH2-O), d3.93 (dd, 1H, J1=12.6 Hz, J2=2.8 Hz, H5''b), d3.93-4.00 (m, 1H, H5'), d3.98 (dd, 1H, J1=J2=10.1 Hz, H5), d4.03 (dd, 1H, J1=10.8 Hz, J2=9.3 Hz, H3'), d4.10 (dd, 1H,

J1=7.2 Hz, J2=4.5 Hz, H3''), d4.13-4.20 (m, 2H, H4, H4''), d4.46 (dd, 1H, J1=4.5 Hz, J2=1.4 Hz Hz, H2''), d5.44 (dd, 1H, J1=1.4 Hz, H1''), d6.05 (dd, 1H, J1=4 Hz, H1'); 13C NMR (CDCl3, 125 MHz): d 29.5 (C2), 40.8 (NH2CH2CH2-O), 41.5 (C6'), 49.9 (C3), 51.3 (C1), 55.0 (C2'), 62.2 (C5''), 67.5 (NH2CH2CH2-O), 69.5 (C3'), 70.9 (C5'), 72.0 (C4'), 74.0 (C6), 74.9 (C2''), 76.8 (C4), 78.3 (C3''), 82.7 (C4''), 86.2 (C5), 97.1 (C1'), 112.0 (C1''); MS: for C19H39N5O10 (M+H): calcd. 498; found 498, for C19H39N5O10 (M-H): calcd. 496; found 496.

Synthesis of 1,6-Anhydro-2,3,4-Tri-O-benzyl idopyranoside (2800) as illustrated in Figure 30. α-O-Methyl-2,3,4-O-benzyl, 5,6- anhydro glucopyranoside (2500) (5.62 g, 12.098 mmol) was dissolved in THF (20 mL) and cooled in an ice/water bath. The reaction was then treated with a 1M solution of BH3.THF in THF (50.9 mL, 50.9 mmol). The hydroboration was complete after an hour and the reaction mixture was then slowly dripped into a cooled flask containing concentrated HOOH (18.1 mL) in 1 N NaOH (181 mL). The aqueous layer was extracted 3 times with EtOAc and the organic phases were back extracted with water. The EtOAc solution was dried over MgSO4 and the solvent was removed. The residue was dissolved in 50 mL of AcOH and treated with 10 drops of 12 N HCl. The reaction was warmed to 70 °C and allowed to proceed for 1 hr, after which time the solvent was removed and the residue was purified by column chromatography over 200 mL of silica gel using 10% to 12.5% to 15% EtOAc in hexane to obtain 2.74 g, 51% or 80 % per step of the product as an oil which solidifies upon standing under vacuum. 2,3,4-Tri-O-benzyl-a-methyl glucopyranoside (2800). H1 NMR (CDCl3, 500 MHz): d1.63 (dd, 1H, J1=7.5 Hz, J2=5.5 Hz, OH), d3.36 (s, 3H, OCH3), d3.50 (dd, 1H, J1=9.5 Hz, J2=3.5 Hz, H2), d3.52 (dd, 1H, J1=J2=9.5 Hz, H4), d3.62- 3.67, (m, 1H, H6a), d3.67- 3.72,

(m, 1H, H5), d3.74- 3.79, (m, 1H, H6b), d4.01 (dd, 1H, J1=J2=9.5 Hz, H3), d4.56 (d, 1H, J= 3.5 Hz, H1), d4.65 (dd, 1H, J1=J2=12 Hz, PhCH2O), d4.85 (dd, 1H, J1=J2=11.5 Hz, PhCH2O), d4.92 (ABq, 2H, J=11 Hz, Dn=49.3 Hz, PhCH2O), d7.25-7.40, (m, 15H, C6H5); 13C NMR (CDCl3, 125 MHz): d 55.2, 61.8,70.6, 73.4, 75.0, 75.8, 79.9, 81.9, 98.1, 127.6, 127.9, 128.0, 128.1, 128.4, 128.5, 138.1, 138.7; HRMS for C28H32O6 (M+Cs): calcd. 597.1253; found 597.1265. 2,3,4-Tri-O-benzyl-b-methyl idopyranioside (27). H1 NMR (CDCl3, 500 MHz): d2.74 (dd, 1H, J1=9 Hz, J2=5 Hz, OH), d3.48 (dd, 1H, J1=8 Hz, J2=3 Hz, H2), d3.48 (s, 3H, OCH3), d3.64 (dd, 1H, J1=8 Hz, J2=5.5 Hz, H4), d3.80-3.87, (m, 1H, H6a), d3.88- 3.94, (m, 1H, H6b), d3.97 (ddd, 1H, J1=J2=J3=5.5 Hz, H5), d4.05 (dd, 1H, J1=J2=8 Hz, H3), d4.53 (d, 1H, J= 3 Hz, H1), d4.54- 4.83, (m, 6H, PhCH2O), d7.25- 7.40, (m, 15H, C6H5); 13C NMR (CDCl3, 125 MHz): d 56.9, 63.1, 73.7, 73.8, 74.9, 75.0, 76.9, 77.8, 78.2, 99.9, 127.8, 127.9, 128.0, 128.1, 128.4, 128.5, 137.7, 138.2, 138.3; HRMS for C28H32O6 (M+Na): calcd. 465.2277; found 487.2108. 1,6-Anhydro-2,3,4-Tri-O-benzyl idopyranoside (28) H1 NMR (CDCl3, 500 MHz): d3.48 (dd, 1H, J1=8 Hz, J2=1.5 Hz, H2), d3.66- 3.75, (m, 2H, H4, H6a), d3.78 (dd, 1H, J1=J2=8 Hz, H3), d4.13 (d, 1H, J= 8 Hz, H6b), d4.39 (dd, 1H, J1=J2=4.5 Hz, H5), d4.60- 4.88, (m, 6H, PhCH2O), d5.30 (d, 1H, J= 1.5 Hz, H1), d7.25- 7.40, (m, 15H, C6H5); 13C NMR (CDCl3, 125 MHz): d 65.5, 73.0, 73.1, 73.2, 75.5, 79.3, 81.8, 82.4, 99.6, 127.6, 127.7, 127.9, 128.0, 128.3, 128.4, 128.5, 137.9, 138.0, 138.6; HRMS for C27H28O5 (M+Cs): calcd. 565.0991; found 565.1015.

Synthesis of 2,3,4-Tri-O-benzyl-1-deoxy-1-b-thiomethyl idopyranoside (3000) as illustrated in Figure 30. Compound 2800 (1.31 g, 2.820 mmol) was dissolved in 15 mL of CH2Cl2 and treated with (methylthio)trimethylsilane (1.07 g, 8.460

mmol) and trimethylsilyl trifluoromethanesulfonate (1.25 g, 5.640 mmol) and stirred for 40 h. The reaction was then quenched by addition of an excess of triethylamine and was subsequently treated with a 1M solution of TBAF in THF (15 mL). After the desilylation was complete, the reaction was diluted wtih EtOAc and extracted 3 times with 1 N NaOH and once with water. The EtOAc solution was dried over MgSO4 and the solvent was removed. The residue was purified by column chromatography over 100 mL of silica gel using 30% to 35% to 40% to 45% EtOAc in hexane to obtain the α anomer first (70 mg, 5%) and then the β anomer (1.20 g, 88.5%). 2,3,4-Tri-O-benzyl-1-deoxy-1-a-thiomethyl idopyranioside (2900) H1 NMR (CDCl3, 500 MHz): d2.17 (s, 3H, SCH3), d3.51 (dd, 1H, J1=J2=4.5 Hz, H2), d3.55 (dd, 1H, J1=J2=4.5 Hz, H3), d3.71 (dd, 1H, J1=12 Hz, J2=4.5 Hz, H6a), d3.76 (dd, 1H, J1=J2=4.5 Hz, H3), d3.94 (dd, 1H, J1=12 Hz, J2=7 Hz, H6b), d4.30- 4.35, (m, 1H, H5), d4.40- 4.78, (m, 6H, PhCH2O), d5.13 (d, 1HJ= 4 Hz, H1), d7.20- 7.40, (m, 15H, C6H5); 13C NMR (CDCl3, 125 MHz): d 14.3, 62.0, 69.6, 72.6, 73.2, 75.4, 75.7, 77.1, 83.6, 127.8, 127.9, 128.1, 128.2, 128.4, 128.5, 137.6, 137.7, 137.8. 2,3,4-Tri-O-benzyl-1-deoxy-1-b-thiomethyl idopyranioside (30) H1 NMR (CDCl3, 500 MHz): d1.89 (dd, 1H, J1=9.5 Hz, J2=3.5 Hz, OH), d2.24 (s, 3H, SCH3), d3.25-3.27 (m, 1H, H4), d3.51-3.57 (m, 2H, H2, H6a), d3.66 (dd, 1H, J1=J2=3 Hz, H3), d3.83 (ddd, 1H, J1=8 Hz, J2=4 Hz, J3=2 Hz, H6b), d4.00 (ddd, 1H, J1=11.5 Hz, J2=8 Hz, J3=3.5 Hz, H5), d4.22-4.39 (m, 3H, PhCH2O), d4.55-4.64 (m, 3H, PhCH2O), d4.79 (d, 1H, J= 1.5 Hz, H1), d7.14- 7.38, (m, 15H, C6H5); 13C NMR (CDCl3, 125 MHz): d 14.7, 62.7, 70.7, 71.7, 71.8, 72.1, 73.2, 75.3, 77.2, 85.1, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 137.4, 137.6, 137.7; HRMS for C28H32O5S (M+Cs): calcd. 613.1025; found 613.1051.

2,3,4-Tri-O-benzyl-1-deoxy-1-b-thiomethyl-6-deoxy-6-allyloxy idopyranoside (3100)as illustrated in Figure 30. Compound 3000 (245 mg, 510 mmol) was dissolved in 3 mL of DMF and treated with NaH (24 mg, 1.02 mmol) followed by allyl bromide (185 mg, 1.53 mmol). After stirring overnight, the reaction was quenced by additon of MeOH and the solvent was removed in vacuo. The resulting residue was partitioned between EtOAc and H2O. The organic phases were then dried over MgSO4 and the solvent was removed. Chromatography over 50 mL of silica gel using a gradient of 15% to 20% to 25% EtOAc in hexane afforded 160 mg, 60% of the title compound. H1 NMR (CDCl3, 500 MHz): d 2.22 (s, 3H, SCH3), d3.34-3.47 (m, 1H, H4), d3.45-3.48 (m, 1H, H2), d3.60-3.65 (m, 2H, H3, H6a), d3.71 (dd, 1H, J1=10 Hz, J2=6 Hz, H6b), d3.92-3.97 (m, 2H, H3, CH2CHCH2O), d3.99-4.05 (m, 1H, CH2CHCH2O), d4.28 (s, 2H, PhCH2O), d4.31 (ABq, 2H, J=12 Hz, Dn=49.7 Hz, PhCH2O), d4.51-4.58 (m, 2H, PhCH2O), d4.77 (d, 1H, J=1.5 Hz, H1), d5.12-5.28 (m, 2H CH2CHCH2O), d5.82-5.92 (m, 1H, CH2CHCH2O), d7.05-7.38 (m, 15H, C6H5); 13C NMR (CDCl3, Bruker AMX-500): d 14.5, 69.5, 71.0, 71.8, 71.9, 72.1, 72.3, 73.0, 75.1, 76.2, 84.9, 116.8, 127.7, 127.8, 127.9, 128.2, 128.4, 128.5, 134.8, 137.8, 138.0, 138.1; HRMS for C31H36O5S (M+Cs): calcd. 653.1338; found 653.1366.

Synthesis of 2,3,4-Tri-O-benzyl-1-deoxy-1-b-thiomethyl-6-deoxy-6-allylamino idopyranoside (3200) as illustrated in Figure 30. DMSO (1.3g, 3.39 mmol) was dissolved in CH2Cl2 (20 mL) and cooled to -78 °C. The reaction was treated with 2 M oxalyl chloride in CH2Cl2 (2.21 mL, 4.42 mmol) and the reaction was allowed to stir for 15 min. Then, a solution of compound 3000 (1.63g, 3.39 mmol) in CH2Cl2 (10 mL) was added dropwise via syringe. The reaction was allowed to proceed at -78°C for 45 min. then triethylamine (1.72 g, 16.96 mmol), was

added and the reaction was allowed to warm up to room temperature. The reaction was diluted with EtOAc and extracted twice with water. The organic phases were dried over MgSO4 and the solvent was removed. The residue was dissolved in methanol (15 mL). A solution of allylamine (1.94 g, 33.9 mmol) was neutralized to pH 6 (pH paper) using glacial acetic acid and this solution was added to the solution of the aldehyde. The reaction was then treated with NaCNBH3 (213 mg, 3.4 mmol). The transformation was complete within 15 minutes. The solvent was removed and the reaction was taken up in EtOAc. The organic phases were dried over MgSO4 and the solvent was removed. The residue was purified by column chromatography over 100 mL of silica gel using 5% to 6% to 7% MeOH in CHCL3 to obtain 1.20 g, 68 %. of the title compound as an oil. H1 NMR (CDCl3, 500 MHz): d 2.23 (s, 3H, SCH3), d2.53 (dd, 1H, J1=12.5 Hz, J2=3.5 Hz, H6a), d3.16 (dd, 1H, J1=12.5 Hz, J2=9 Hz, H6b), d3.18-3.26 (m, 3H, H4 and CH2CHCH2O), d3.49-3.51 (m, 1H, H2), d3.66 (dd, 1H, J1=J2=3 Hz, H3), d3.87-3.92 (m, 1H, H5), d4.26-4.61 (m, 6H, PhCH2O), d4.78 (d, 1H, J= 1.5 Hz, H1), d5.03-5.17 (m, 2H, CH2CHCH2O), d5.78-5.88 (m, 1H, CH2CHCH2O), d7.14- 7.38, (m, 15H, C6H5); 13C NMR (CDCl3, 125 MHz): d 14.7, 49.6, 52.2, 70.8, 71.8, 72.0, 72.6, 73.2, 75.3, 75.9, 85.2, 116.2, 127.7, 127.8, 128.0, 128.3, 128.4, 128.5, 136.5, 137.5, 137.9; HRMS for C31H37NO4S (M+Na): calcd. 542.2341; found 542.2353.

Synthesis of 2,3,4-Tri-O-benzyl-1-deoxy-1-b-thiomethyl-6-deoxy-6-carbobenzyloxyamido idopyranoside (3300). Compound 3200 (894 mg, 1.72 mmol) was dissolved in a mixture of acetonitrile and water (84/16) and brought to reflux. A system was set up such that the solvent in the pot was continuously being distilled off while fresh acetonitrile/water mixture was added to replace the

distillate. A suspension of Wilkinson's catalyst (300 mg, 1.720 mmol) in the acetonitrile/water mixture was added and the reaction was allowed to reflux vigorously. The reaction was complete in 2 h and the solvent was removed. The residue was dissolved in CH2Cl2 and cooled with an ice bath. The reaction was then treated with a solution of N-benzyloxycarbonyloxy succinimide (536 mg, 2.15 mmol) in CH2Cl2 (5 mL). The reaciton was complete within 15 minutes. The solvent was removed and the residue was chromatographed over 100 mL of silica gel using 17.5% to 20% to 22.5% to 25 % EtOAc in hexane to afford 706 mg, 67% of the title compound as a colorless oil. H1 NMR (CDCl3, 500 MHz): d 2.20 (s, 3H, SCH3), d3.20-3.23 (m, 1H, H4), d3.34-3.41 (m, 1H, H6a), d3.44-3.52 (m, 2H, H6b, H2), d3.64 (dd, 1H, J1=J2=2.5 Hz, H3), d3.79-3.84 (m, 1H, H5), d4.20-4.36 (m, 3H, benzillic protons), d4.52-4.61 (m, 3H, PhCH2O), d4.74 (s, 1H, H1), d4.86-4.91 (m, 1H, CH2-NHZ), d5.02-5.1 (m, 2H, PhCH2O), d7.13-7.20 (m, 4H, C6H5), d7.26-7.37, (m, 16H, C6H5); 13C NMR (CDCl3, 125 MHz): d 14.6, 41.8, 66.6, 70.4, 71.7, 71.8, 72.0, 73.2, 75.1, 75.3, 85.0, 127.9, 128.0, 128.3, 128.4, 128.5, 136.6, 137.3, 137.5, 137.8, 156.4; HRMS for C36H39NO6S (M+Cs): calcd. 746.1552; found 746.1568.

Synthesis of Compound 34 as illustrated in Figure 31. Compound 2000 (69.4 mg, 69 mmol) and 31 (97 mg, 186 mmol) were mixed and dried overnight over P2O5. Then CH2Cl2 (5mL) was added via syringe. The reaction was cooled to -10 °C using an ice/salt bath and NIS (46 mg, 20 mmol) was added. The reaction was allowed to stir for 15 min. and then a catalytic amount of AgOTf (~2 mg) was added. The reaction assumed a purple color and was allowed to proceed for 45 min before quenching with triethylamine. The reaction was then filtered through a pad of celite and the solvent was removed.

Chromatography of the residue over 50 mL of silica gel using a gradient of 10% to 15% to 20 % to 25% ethyl acetate in hexane afforded 50 mg, 49% of the desired product. 1H NMR (CDCl3, 500 MHz): d1.42 (ddd, 1H, J1=J2=J3=12.5 Hz, H2 eq), d2.24 (ddd, 1H, J1=12.5 Hz, J2=J3=4.5 Hz, H2 ax), d3.10 (dd, 1H, J1=10.5 Hz, J2=4 Hz), d3.22-3.32 (m, 4H), d3.36-3.48 (m, 4H), d3.10 (dd, 1H, J1=10 Hz, J2=5.5 Hz), d3.59 (dd, 1H, J1=J2=3.5 Hz), d3.61-3.67 (m, 2H), d3.83 (dd, 1H, J1=10.5 Hz, J2=2 Hz), d3.84-3.97 (m, 5H), d4.00 (dd, 1H, J1=J2=9.5 Hz), d4.10-4.25 (m, 4 H), d4.34-4.61 (m, 10H), d4.67-4.75 (m, 3H), d4.76-4.89 (m, 3H), d4.93 (d, 1H, J=11 Hz), d5.11-5.16 (m, 1H), d5.19-5.27 (m, 1H), d5.55 (d, J=4.5 Hz, 1H, H1''), d5.79-5.89 (m, 1H), d6.14 (d, 1H, J=4 Hz, H1'), d7.02-7.37 (m, 40H); 13C NMR (CDCl3, 125 MHz): d 32.4, 51.2, 59.8, 60.4, 63.2, 69.4, 70.2, 70.8, 71.9, 72.1, 72.2, 72.4, 72.6, 73.2, 73.9, 74.0, 74.1, 74.8, 75.2, 75.3, 75.4, 76.5, 78.5, 80.1, 81.8, 82.0, 82.3, 83.9, 95.6, 100.5, 107.0, 116.9, 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 128.0, 128.1, 128.2, 128.4, 128.5, 134.8, 137.6, 137.7, 137.82, 137.84, 138.0, 138.4, 138.8; HRMS: for C82H89N12O15 (M+Cs): calcd. 1614.5625; found 1614.5539.

Synthesis of compound 3500 as illustrated in Figure 31. Bis (methyldiphenylphoshino)cyclooctadienyl IrI hexafluorophosphate (5 mg, 6 mmol) was suspended in THF (5mL) and H2 was bubbled through this suspension for 20 minutes. The resulting crear solution was transferred via syringe into a solution of compound 3400 (50 mg., 34 mmol) in THF (15 mL). After 1 hr, a quantitative conversion to a slightly less polar material was observed. The solvent was removed and the residue was co-evaporated with CH2Cl2 several times. The reaction was then taken up in CH2Cl2 (30 mL) and treated with trimethylamine N-oxide dihydrate (19 mg, .17 mmol), and a

solution of OsO4 in tBuOH (20 mL of the 2.5 wt.% commercial preparation). After the reaction was over (overnight) the solvent was removed and the residue was purified over 50 mL of silica gel using 15% to 20% to 25% to 30% EtOAc in hexane to obtain 41 mg, 84% of the title compound. 1H NMR (CDCl3, 500 MHz): d1.41 (ddd, 1H, J1=J2=J3=16 Hz, H2 eq), d2.24 (ddd, 1H, J1=16 Hz, J2=J3=5.5 Hz, H2 ax), d2.70-2.82 (m, 1H, OH), d3.15-3.23 m, 2H), d3.25-3.43 (m, 6H), d3.47 (dd, 1H, J1=16.5 Hz, J2=2.5 Hz), d3.47-3.57 (m, 1H), d3.59 (dd, J1=J2=11.5 Hz, 1H), d3.63-3.77 (m, 4H), d3.78-3.84 (m, 1H), d3.89-4.03 (m, 3H), d4.15-4.21 (m, 1H), d4.23-4.49 (m, 8H), d4.52-4.72 (m, 7H), d4.78-4.90 (m, 4H), d5.52 (d, 1H, J=4.5 Hz, H1''), d5.98 (d, 1H, J=4.5 Hz), d7.06-7.37 (m, 40H); 13C NMR (CDCl3, 125 MHz): d 32.3, 51.1, 59.6, 60.4, 62.6, 63.3, 69.3, 70.9, 72.1, 72.3, 73.0, 73.6, 74.0, 74.7, 74.9, 75.1, 75.4, 75.8, 76.0, 78.4, 80.0, 81.3, 81.5, 81.9, 83.4, 95.9, 99.9, 107.4, 127.3, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 137.65, 137.69, 137.8, 137.9, 138.0, 138.6; HRMS: for C79H85N12O15 (M+Cs): calcd. 1574.5312; found 1574.5397.

Synthesis of 2''', 6'''-desamino-2'''-6'''-hydroxy neomycin B (700) as illustrated in Figure 31. The deprotection of 3500 (31 mg, 2.15 mmol) was carried out in the exact manner as the preparation of compound 6 to afford 12.4 mg, 76% of 704 HCl. 1H NMR (D2O, adjusted with DCl, 600 MHz): d1.85 (ddd, 1H, J1=J2=J3=12.6 Hz, H2 eq), d2.24 (ddd, 1H, J1=12.6 Hz, J2=J3=4.1 Hz, H2 ax), d3.24 (dd, 1H, J1=13.7 Hz, J2=6.3 Hz, H6'a), d3.32 (ddd, 1H, J1=12.6 Hz, J2=10.6 Hz, J3=4.1 Hz, H1), d3.37-3.43 (m, 2H, H2', H6'b), d3.43 (dd, 1H, J1=J2=9.4 Hz, H4'), d3.51 (ddd, 1H, J1=12.6 Hz, J2=10.3 Hz, J3=4.1 Hz, H3), d3.57-3.60 (m, 1H, H4'''), d3.65 (dd, 1H, J1=10.6 Hz, J2=9.2 Hz, H6), d3.72-3.82 (m, 4H, H6'''a, H6'''b, H5''a,

H2'''), d3.85-3.97 (m, 5H, H5''b, H5', H5, H3', H5'''), d3.99 (dd, 1H, J1=J2=3.7 Hz, H3'''), d4.06 (dd, 1H, J1=10.3 Hz, J2=9.2 Hz, H4), d4.14-4.18 (m, 1H, H4''), d4.35 (dd, 1H, J1=4.7 Hz, J2=1.7 Hz, H2''), d4.42 (dd, 1H, J1=7.2 Hz, J2=4.7 Hz, H3''), d4.89 (d, 1H, J=1.3 Hz, H1'''), d5.35 (d, 1H, J=1.7 Hz, H1''), d5.98 (d, 1H, J=4 Hz, H1'); 13C NMR (CDCl3, 125 MHz): d 29.5 (C2), 41.5 (C6'), 49.9 (C3), 51.3 (C1), 55.0 (C2'), 62.8 (C5'' and (C2''' or C2''')), 69.46 (C4'''), 69.52 (C3'), 70.7 (C2''' or C6'''), 70.9 (C5'), 71.1 (C3'''), 72.0 (C4'), 74.0 (C6), 75.3 (C2''), 76.8, 76.9 (C3'', C4, C5'''), 83.0 (C4''), 86.1 (C5), 97.1 (C1'), 100.3 (C1'''), 111.6 (C1''); MS: for C23H44N4O15 (M+H): calcd. 617; found 617, for C23H45N5O14 (M-H): calcd. 615; found 615.

Synthesis of compound 3600 as illustrated in Figure 31. Compound 2000 (321 mg, .32 mmol) and compound 3300 (312 mg, .510 mmol) were dried together with 3 Å MS (250 mg) overnight. Then CH2Cl2 (5 mL) was added and the reaction was cooled to -10 °C using an ice/salt bath. After stirring for 30 min, NIS (125 mg, .56 mmol) was added and the reaction was allowed to stir for 15 min Then, a catalytic amount of AgOTf was added and the reaction was allowed to stir for 30 min. prior to quenching with triethylamine. The reaction was then filtered through a pad of celite and the solvent was removed. Chromatography of the residue over 50 mL of silica gel using a gradient of 10% to 15% to 20 % to 25% ethyl acetate in hexane afforded 175 mg, 35%. of the desired product. 1H NMR (CDCl3, 500 MHz): d1.35 (ddd, 1H, J1=J2=J3=12.5 Hz, H2 eq), d2.17 (ddd, 1H, J1=12.5 Hz, J2=J3=4.5 Hz, H2 ax), d3.12 (dd, J1=10 Hz, J2=3.5 Hz, 1H, H2'), d3.15 (dd, J1=J2=9 Hz, 1H, H3'''), d3.21-3.33 (m, 3H, H1, H3, H4'''), d3.29 (dd, 1H, J1=13.5 Hz, J2=4.5 Hz, H6'a), d3.34-3.49 (m, 4H, H5, H4', H6'''a, H6'''b), d3.47 (dd, 1H, J1=13.5 Hz, J2=2.5 Hz, H6'b),

d3.55-3.72 (m, 5H, H4, H6, H5''a, H5''b, H2'''), d3.77-3.83 (m, 1H, H5'''), d3.95 (dd, 1H, J1=4.5 Hz, J2=4 Hz, H2''), d4.00 (dd, 1H, J1=10 Hz, J2=9.5 Hz, H3'), d4.13-4.19 (m, 1H, H5'), d4.19-4.24 (m, 2H, H3'', PhCH2O), d4.29-4.34 (m, 2H, H4'', PhCH2O), d4.38-5.12 (m, 17H, PhCH2O and H1'''), d5.47-5.53 (m, 1H, CbzNH), d5.54 (d, 1H, J1=4 Hz, H1''), d5.99 (d, 1H, J1=3.5 Hz, H1'), d7.02-7.37 (m, 40 H, C6H5); 13C NMR (CDCl3, 125 MHz): d 32.2, 41.6, 51.2, 59.6, 60.3, 63.2, 66.5, 69.4, 70.9, 71.7, 72.4, 72.6, 73.3, 73.89, 73.93, 74.2, 74.3, 74.9, 75.1, 75.3, 75.8, 76.6, 78.5, 79.9, 81.3, 81.5, 82.1, 83.4, 95.9, 100.1, 107.2, 127.2, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5, 136.6, 137.56, 137.60, 137.80, 137.81, 138.1, 138.6, 156.5; HRMS for C87H91N13O16 (M+Cs): calcd, 1706.5761; found, 1706.5849.

Synthesis of 2'''-desamino-2'''-hydroxy neomycin B (800) as illustrated in Figure 31. The deprotection of compound 3600 (60.7 mg, 39 mmol) was carried out in the exact manner as the preparation of compound 6 to afford 21.6 mg, 70% of 805 HCl. 1H NMR (D2O, pD 2 adjusted with DCl, Bruker AMX-500): d1.95 (ddd, 1H, J1=J2=J3=12.6 Hz, H2 eq), d2.24 (ddd, 1H, J1=12.6 Hz, J2=J3=4.1 Hz, H2 ax), d3.33 (dd, 1H, J1=13.7 Hz, J2=6.4 Hz, H6'a), d3.35-3.44 (m, 3H, H6'''a, H1, H6'''b), d3.46-3.51 (m, 2H, H2', H6'b), d3.52 (dd, 1H, J1=J2=9.3 Hz, H4'), d3.60 (ddd, 1H, J1=12.8 Hz, J2=10.2 Hz, J3=4.1 Hz, H3), d3.71-3.74 (m, H4'''), d3.77 (dd, 1H, J1=10.4 Hz, J2=9.3 Hz, H6), d3.80 (dd, 1H, J1=12.4 Hz, J2=5.1 Hz, H5''a), d3.85-3.88 (m, 1H, H2'''), d3.95 (dd, 1H, J1=12.4 Hz, J2=3.0 Hz, H5''b), d3.94-3.99 (m, 1H, H5'), d3.99 (dd, 1H, J1=10.2 Hz, J2=9.3 Hz, H5), d4.04 (dd, 1H, J1=10.9 Hz, J2=9.3 Hz, H3'), d4.11 (dd, 1H, J1=J2=3.5 Hz, H3'''), d4.18 (dd, 1H, J1=J2=10.2 Hz, H4), d4.23-4.28 (m, 2H, H4'', H5'''), d4.44 (dd, 1H, J1=4.8 Hz, J2=2.4 Hz, H2''), d4.52 (dd, 1H, J1=6.5 Hz, J2=4.8 Hz, H3''),

d5.03 (d, 1H, J=1.2 Hz, H1'''), d5.46 (d, 1H, J=2.4 Hz, H1''), d6.09 (d, 1H, J=4 Hz, H1'); 13C NMR (CDCl3, 125 MHz): d 29.5 (C2), 41.6 (C6'), 42.0 (C6'''), 49.9 (C3), 51.3 (C1), 54.9 (C2'), 61.8 (C5''), 69.5 (C3'), 70.0 (C4'''), 70.2 (C2'''), 70.9 (C5'), 71.0 (C3'''), 72.01 (C4'), 72.04 (C5'''), 73.9 (C6), 75.2 (C2''), 76.7 (C4), 76.9 (C3''), 83.1 (C4''), 86.3 (C5), 97.0 (C1'), 100.1 (C1'''), 111.7 (C1''); MS: for C23H45N5O14 (M+H): calcd. 616; found 616, for C23H45N5O14 (M-H): calcd. 614; found 614.

General Procedures for SPR Binding Studies done in Example 5. Samples were prepared by serial dilutions from stock solutions in RNase free microfuge tubes (Ambion) and were centrifuged at 14000 rpm for degassing. Unless otherwise noted, all binding studies were carried out using HBS buffer (Pharmacia Biosensor AB) which was used as obtained. All procedures for binding studies were automated as methods using repetitive cycles of sample injection and regeneration. Typically, buffer was injected in the first two cycles to establish a stable baseline value. Samples were injected at a flowrate of 5-10 mL/min using either the KINJECT command. All aminoglycoside samples were injected from autoclaved 7 mm plastic vials that were capped with pierceable plastic crimp caps. To minimize carry over, samples were injected in order of increasing concentration. The running buffer was identical to the injection buffer. Expected values for the equilibrium response of one equivalent of analyte were calculated from the relative molecular weight of the analyte and the immobilized RNA ligand in each flowcells and adjusted with a correction factor of 0.76 which arises from the different molar refractive indices of RNA and the analyte. Binding constants were calculated by fitting the recorded binding isotherm (equivalents bound vs, concentration) to a

model with n independent binding constants using the fitting program provided in the program Kaleidagraph (Macintosh).

Neomycin B sulfate (Fluka) was converted to the free base by passing it through Amberlite IRA 400 (OH- form) and purified by ion exchange chromatography on Dowex 1-X2 100 to remove neomycin C;23 the purity of neomycin B was verified by NMR in D2O. Neamine was obtained by acid catalyzed cleavage of neomycin B and purified by ion exchange chromatography on Amberlite CG-50. Paromamine was obtained by acid catalyzed cleavage of paromomycin and purified in the same manner. Paromomycin sulfate, kanamycin A, kanamycin B and streptomycin were obtained from Sigma and used as received. Tobramycin, gentamicin, apramycin, ribostamycin, butirosin and hygromycin B were obtained from Fluka and used as received. 2'''-hydroxy-neomycin B, 2''',6'''-dihydroxy-neomycin B and derivatives of ribostamycin were obtained via total synthesis.

General Procedure for Ozonolysis of Compounds 6000-8000 as shown in Figure 58: (For each library compound to be produced, 0.15 mmol of the 2-acylamido-glucosamine derivative was used.) A solution of compounds 6000-9000 in a total of 7 mL of a MeOH:CH2Cl2 mixture (containing only as much CH2Cl2 as needed for solubility) was cooled to -78°C and treated successively with oxygen, then ozone (until the faint blue color was visible) and then oxygen again. After all remaining ozone had been purged, dimethylsulfide was added (200 uL, 3 mmol) and the solution allowed to warm to ambient temperature (circa 1h). The solvent was evaporated and the product dried for 1h under high vacuum. The crude aldehdes 9000-11000 were then used in the reductive amination.

General Procedure for Reductive Amination of Compounds 9000-11000 as shown in Figure 58: The aldehydes 9000-11000 (0.15 mmol) were dissolved in 1 mL MeOH and treated first with 0.45 mL of a 1 M solution of the amine in MeOH, then with 0.5 mL of a 1 M solution of acetic acid in MeOH, and finally with 0.22 mL of a freshly prepared 0.3 M solution of NaCNBH3 in MeOH. (If an amine hydrochloride salt was used instead of a free amine, water was added to the amine solution as needed for solubility, the amount of AcOH solution was reduced to 0.05 mL and the amount of NaCNBH3 solution was increased to 0.25 mL.) After 2h, water was added (0.5 mL) and stirring was continued for 20 min, after which time the mixture was evaporated. The crude products 12000-14000 were used without further purification in the hydrogenation step.

General Procedure for Hydrogenation of Compounds 12000-14000 a-f as shown in Figure 58: A solution of compounds 12000-14000 (0.15 mmol) in 3 mL AcOH and 2 mL water was degassed by evacuating and refilling with argon several times. Hydrogenation catalyst (20% Pd(OH)2 on carbon, wet Degussa type, circa 20 mg) was added, the flask carefully evacuated and then refilled with hydrogen from a balloon. The needle connected to the balloon was inserted into the solution and hydrogen was allowed to bubble though the solution for circa 3 min by piercing the septum with another needle. Then the flask was kept under positive hydrogen pressure and stirred for 3-12 h until reduction was complete (TLC of the products in MeOH:conc. NH3 = 9:1 to 3:1, staining with ninhydrin). The balloon was removed and the solution purged with argon. Water was added (5 mL) and the reaction mixture filtered through a celite pad which was washed with 5 mL water. The combined filtrates were evaporated, dissolved

in 2 mL water and applied onto an Amberlite CG-50 column (NH_4^+ form, 16 x 1.5 cm) and eluted with a gradient made from 250 mL water (solution A) and 250 mL water containing 1-30% concentrated aqueous ammonia. Fractions containing 5 mL were collected with an automatic fraction collector and the product-containing fractions were pooled and lyophilized. Hydrochloride salts of the final products were prepared by adding excess 1 M HCl and lyophilizing again. All compounds were characterized by 1H-NMR, 13C-NMR and Electrospray-MS.

Selective Hydrogenation of Compounds 12000-14000 e as shown in Figure 58: Following the hydrogenation procedure as outline above, the reaction was stopped and filtered after 2-3 h (TLC control) and the product isolated by ion exchange chromatography as described above to form compounds 15000-17000 a-g.

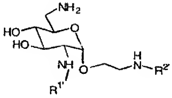
Screening/Surface Plasmon Resonance Binding Assays of Library Compounds as diagramed in Figure 60. Following the general protocols outlined previously, biotinylated RNA sequences were prepared and immobilized on SA5 sensorchips. Binding to three sequences was assayed at once in three parallel flowcells, with the fourth flowcell containing no immobilized RNA serving as a control. Compounds were assayed at four concentrations (100, 31.6, 10, 3.16 mM). Using the known molecular weight of the compounds,the SPR responses for each ligand were normalized and expressed as fraction of equivalents bound to the RNA at each concentration. From this titration curve, the Kd for each compound was estimated from a single appropriate datapoint which represented just under 0.5 bound equivalents assuming a 1:1 binding isotherm.

Automated Method for Library Analysis. The samples were

screened at four concentrations with injection times 4 min 30 s each. After recording three different series,. a control sample of paromomycin is tested to ensure reproducibility. With the available autosampler racks, up to 12 compounds can be screened at once over a period of 24 h.

What is claimed is:

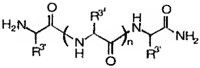
1. A compound represented by the following structure:



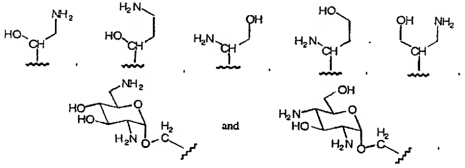
wherein R 1' is selected from a group consisting of a hydrogen radical and amide linked radicals of the following amino acids: Ala, Arg, Asn, Gln, Gly, Ile, Leu, Lys, Phe, Pro, Thr, and Val , and

wherein R 2' is selected from a group consisting of the following radicals -H, propyl, isopropyl, $-(CH_2)_2NH_2$, $-(CH_2)_3NH_2$, $-CH_2CH(NH_2)CH_3$, $-(CH_2)_4NH_2$, $-(CH_2)_6NH_2$, $-(CH_2)_2NH$-Ethyl, $-(CH_2)_2NH(CH_2)_2NH_2$, $-(CH_2)_3NH(CH_2)_3NH_2$, $-(CH_2)_3NH(CH_2)_4NH(CH_2)_3NH_2$, $-(CH_2)_4NH(CH_2)_3NH_2$, $-(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$, $-(CH_2)_2N(CH_2CH_2NH_2)_2$, $-CH_2-C(=O)NH_2$, $-CH(CH_3)-C(=O)NH_2$, $-CH_2$-Ph, -CH(*i*-propyl)$-C(=O)NH_2$, -CH(benzyl)-$C(=O)NH_2$, $-(CH_2)_2OH$, $-(CH_2)_3OH$, and $-CH(CH_2OH)_2$.

2. A compound represented by the following structure:

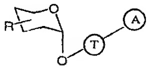


wherein $0 \le n \le 18$ and each $R^{3'}$ is independently selected from the group consisting of side chains of naturally occuring amino acids and radicals represented by the following structures:



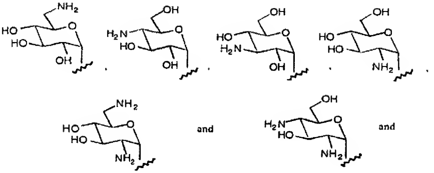
with the proviso that for $0 \le n \le 1$, all of the $R^{3'}$ are selected from said radicals only, and for $2 \le n \le 18$, at least 3 of $R^{3'}$ are selected from said radicals.

3. A compound represented by the following structure:

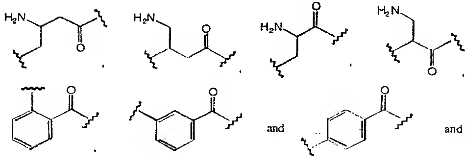


wherein  is selected from a group consisting of

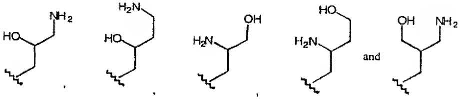
diradicals represented by the following structures:



wherein (T) is selected from a group consisting of radicals represented by the following structures:

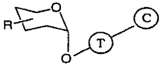


wherein A is selected from a group consisting of radicals represented by the following structures:

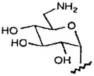
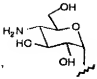
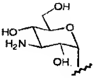
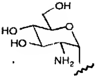


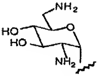
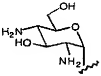
wherein the carbonyl of T is linked to A .

4. A compound represented by the following structure:

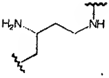
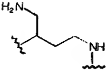
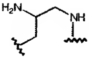
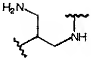


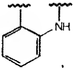
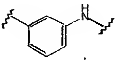
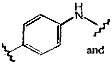
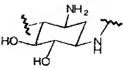
wherein  is selected from a group consistinig of radicals represented by the following structures:

 ,  ,  ,  ,

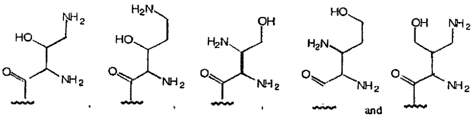
 and  and

wherein T is selected from a group consistinig of diradicals represented by the following structures:

 ,  ,  ,  ,

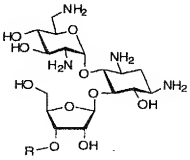
 ,  ,  and  and

wherein C is selected from a group consistinig of radicals represented by the following structures:

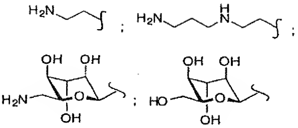


wherein the carbonyl of T is linked to C.

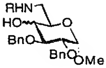
5. A compound represented by the following structure:



wherein R is selected from a group consisting of radicals represented by one of the following structures:

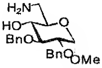


6. A compound represented by the following structure:

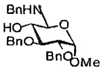


wherein R is selected from the group of radicals consisting of H and benzyl.

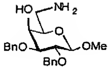
7. A compound as described in claim 6 represented by the following structure:



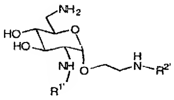
8. A compound as described in claim 6 represented by the following structure:


.

9. A compound as described in claim 6 represented by the following structure:


.

10. A library of compounds having nucleic acid binding hydroxyamine substructures comprising a plurality of compounds represented by the following structure:

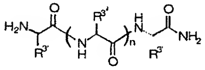


wherein $R^{1'}$ is selected from a group consisting of a hydrogen radical and amide linked radicals of the following

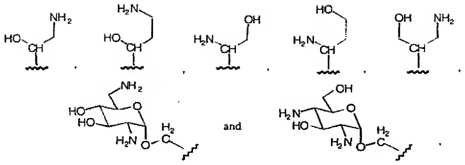
amino acids: Ala, Arg, Asn, Gln, Gly, Ile, Leu, Lys, Phe, Pro, Thr, and Val , and

wherein $R^{2'}$ is selected from a group consisting of the following radicals -H, propyl, isopropyl, $-(CH_2)_2NH_2$, $-(CH_2)_3NH_2$, $-CH_2CH(NH_2)CH_3$, $-(CH_2)_4NH_2$, $-(CH_2)_6NH_2$, $-(CH_2)_2NH$-Ethyl, $-(CH_2)_2NH(CH_2)_2NH_2$, $-(CH_2)_3NH(CH_2)_3NH_2$, $-(CH_2)_3NH(CH_2)_4NH(CH_2)_3NH_2$, $-(CH_2)_4NH(CH_2)_3NH_2$, $-(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$, $-(CH_2)_2N(CH_2CH_2NH_2)_2$, $-CH_2-C(=O)NH_2$, $-CH(CH_3)-C(=O)NH_2$, $-CH_2-Ph$, -CH(*i*-propyl)-C(=O)NH_2, -CH(benzyl)-C(=O)NH_2, $-(CH_2)_2OH$, $-(CH_2)_3OH$, and $-CH(CH_2OH)_2$.

11. A library of compounds having nucleic acid binding hydroxyamine substructures comprising a plurality of compounds represented by the following structure:

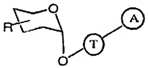


wherein $0 \leq n \leq 18$ and each $R^{3'}$ is independently selected from the group consisting of side chains of naturally occuring amino acids and radicals represented by the following structures:

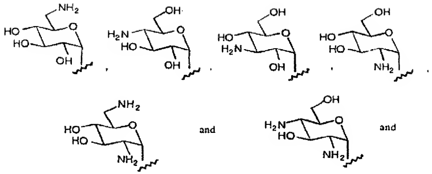


with the proviso that for $0 \leq n \leq 1$, all of the $R^{3'}$ are selected from said radicals only, and for $2 \leq n \leq 18$, at least 3 of $R^{3'}$ are selected from said radicals.

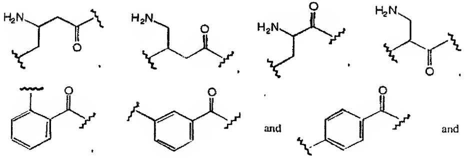
12. A library of compounds having nucleic acid binding hydroxyamine substructures comprising a plurality of compounds represented by the following structure:



wherein  is selected from a group consisting of radicals represented by the following structures:

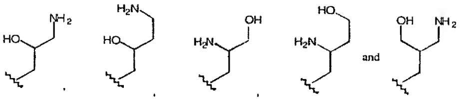


wherein T is selected from a group consisting of diradicals represented by the following structures:



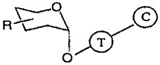
wherein A is selected from a group consistinig of

radicals represented by the following structures:

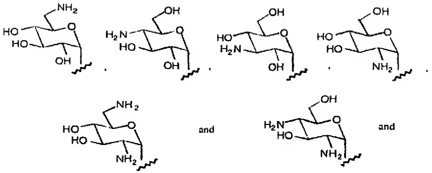


wherein the carbonyl of T is linked to A.

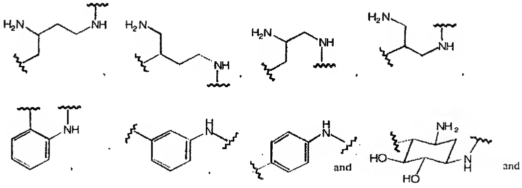
13. A library of compounds having nucleic acid binding hydroxyamine substructures comprising a plurality of compounds represented by the following structure:



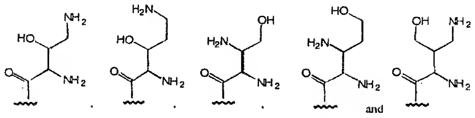
wherein  is selected from a group consistinig of radicals represented by the following structures:



wherein T is selected from a group consistinig of diradicals represented by the following structures:

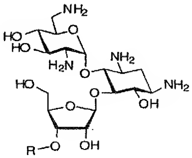


wherein (C) is selected from a group consisting of radicals represented by the following structures:

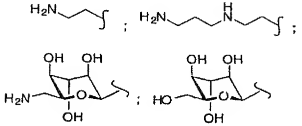


wherein the carbonyl of (T) is linked to (C) .

14 A library of compounds having nucleic acid binding hydroxyamine substructures comprising a plurality of compounds represented by the following structure:



wherein R is selected from a group consisting of a radical represented by one of the following structures:

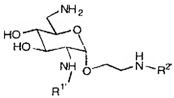


15. A sensorchip having a surface employable for surface plasmon resonance, said surface having immobilized RNA attached thereto.

16. A sensorchip as described in claim 15 wherein said surface is coated with streptavidin, said RNA is biotinylated, and said RNA is immobilized onto said surface by streptavidin/biotin binding.

17. A sensorchip as described in claim 16 wherein bound to said RNA is a compound having a nucleic acid binding hydroxyamine substructure.

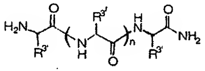
18. A sensorchip as described in claim 17 wherein said compound represented by the following structure:



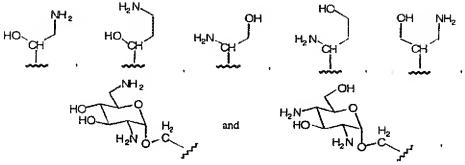
wherein R $^{1'}$ is selected from a group consisting of a hydrogen radical and amide linked radicals of the following amino acids: Ala, Arg, Asn, Gln, Gly, Ile, Leu, Lys, Phe, Pro, Thr, and Val , and

wherein R $^{2'}$ is selected from a group consisting of the following radicals -H, propyl, isopropyl, $-(CH_2)_2NH_2$, $-(CH_2)_3NH_2$, $-CH_2CH(NH_2)CH_3$, $-(CH_2)_4NH_2$, $-(CH_2)_6NH_2$, $-(CH_2)_2NH$-Ethyl, $-(CH_2)_2NH(CH_2)_2NH_2$, $-(CH_2)_3NH(CH_2)_3NH_2$, $-(CH_2)_3NH(CH_2)_4NH(CH_2)_3NH_2$, $-(CH_2)_4NH(CH_2)_3NH_2$, $-(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$, $-(CH_2)_2N(CH_2CH_2NH_2)_2$, $-CH_2-C(=O)NH_2$, $-CH(CH_3)-C(=O)NH_2$, $-CH_2$-Ph, $-CH(i\text{-propyl})-C(=O)NH_2$, $-CH(\text{benzyl})-C(=O)NH_2$, $-(CH_2)_2OH$, $-(CH_2)_3OH$, and $-CH(CH_2OH)_2$.

19. A sensorchip as described in claim 17 wherein said compound represented by the following structure:

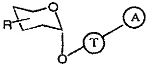


wherein $0 \leq n \leq 18$ and each R $^{3'}$ is independently selected from the group consisting of side chains of naturally occuring amino acids and radicals represented by the following structures:

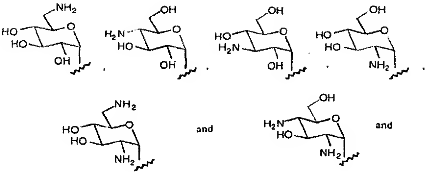


with the proviso that for $0 \leq n \leq 1$, all of the $R^{3'}$ are selected from said radicals only, and for $2 \leq n \leq 18$, at least 3 of $R^{3'}$ are selected from said radicals.

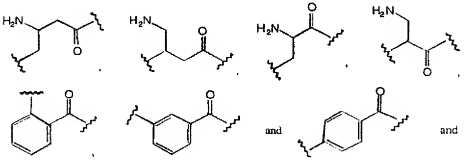
20. A sensorchip as described in claim 17 wherein said compound represented by the following structure:



wherein  is selected from a group consisting of diradicals represented by the following structures:

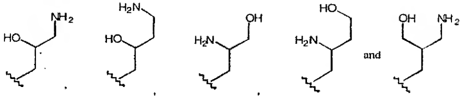


wherein (T) is selected from a group consisting of diradicals represented by the following structures:



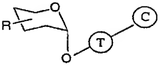
wherein (A) is selected from a group consisting of

radicals represented by the following structures:



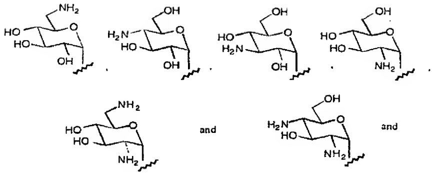
wherein the carbonyl of T is linked to A .

21. A sensorchip as described in claim 17 wherein said compound represented by the following structure:

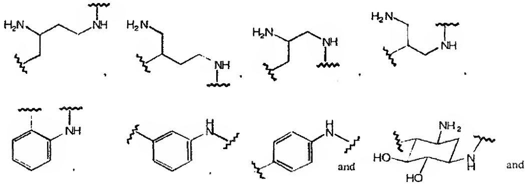


wherein 

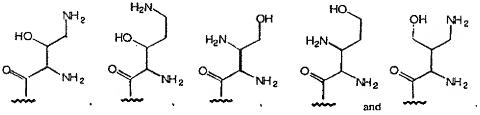
is selected from a group consistinig of radicals represented by the following structures:



wherein (T) is selected from a group consisting of diradicals represented by the following structures:

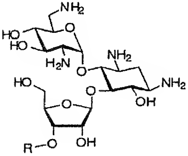


wherein C is selected from a group consisting of radicals represented by the following structures:



wherein the carbonyl of T is linked to C.

22. A sensorchip as described in claim 17 wherein said compound represented by the following structure:



wherein R is selected from a group consisting of a radical represented by one of the following structures:

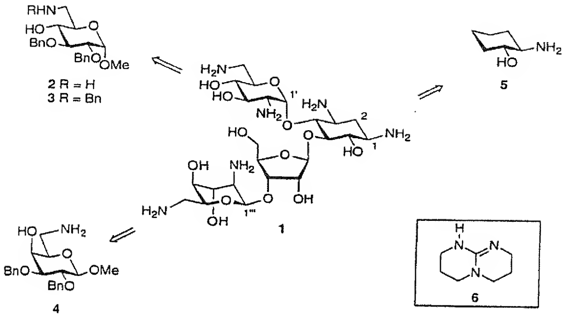

RHN
HO
BnO
BnO
OMe
O
2 R = H
3 R = Bn
H_2N
HO
HO
NH_2
1'
H_2N
2
NH_2
HO
1
OH
NH_2
H_2N
OH
1'''
OH
1
NH_2
HO
5
HO
NH_2
BnO
OMe
BnO
4
H
N
6

FIGURE 1

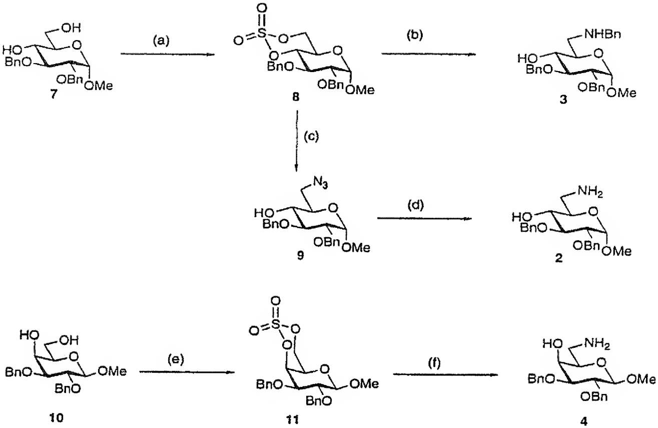

OH
HO
BnO
OBn
OMe
7
(a)
O
O=S-O
O
BnO
OBn
OMe
8
(b)
NHBn
HO
BnO
OBn
OMe
3
(c)
N3
HO
BnO
OBn
OMe
9
(d)
NH2
HO
BnO
OBn
OMe
2
HO
OH
BnO
BnO
OMe
10
(e)
O
O=S-O
O
BnO
BnO
OMe
11
(f)
HO
NH2
BnO
OBn
OMe
4

FIGURE 2

Receptor	Anion	K_a, M^{-1} [a]	$\Delta\delta_{max}$(OH)
2•H^+	Cl^-	49 ± 3	+ 0.11
	$(MeO)_2PO_2^-$	490 ± 12	+ 0.84
3•H^+	Cl^-	36 ± 6	+ 0.09
	$(MeO)_2PO_2^-$	254 ± 27	+ 0.66
4•H^+	Cl^-	51 ± 1	- 0.01
	$(MeO)_2PO_2^-$	132 ± 19	+ 0.38
5•H^+	Cl^-	53 ± 4	+ 0.08
	$(MeO)_2PO_2^-$	230 ± 25	+ 0.56
6•H^+	Cl^-	27 ± 1	N/A
	$(MeO)_2PO_2^-$	342 ± 51	N/A

FIGURE 3

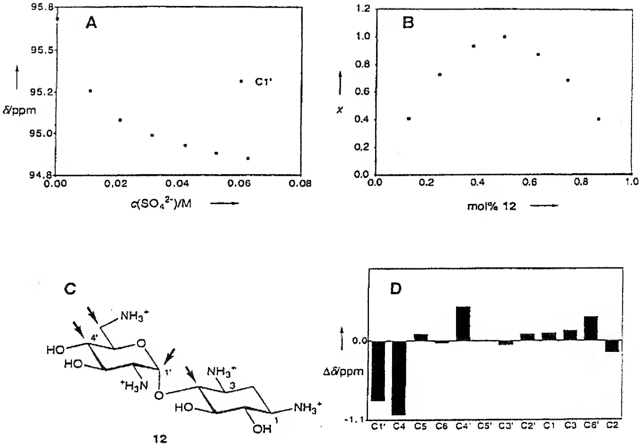

A
95.8
95.5
95.2
95.0
94.8
δ/ppm
C1'
0.00
0.02
0.04
0.06
0.08
c(SO$_4^{2-}$)/M
B
1.2
1.0
0.8
0.6
0.4
0.2
0.0
x
0.0
0.2
0.4
0.6
0.8
1.0
mol% 12
C
NH$_3^+$
4'
HO
O
HO
1'
NH$_3^+$
$^+$H$_3$N
3
O
HO
NH$_3^+$
OH
1
12
D
0.0
Δδ/ppm
-1.1
C1'
C4
C5
C6
C4'
C5'
C3'
C2'
C1
C3
C6'
C2

FIGURE 4

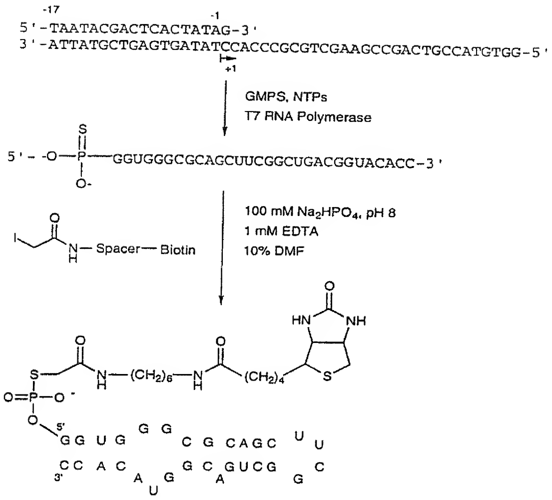

-17
-1
5'-TAATACGACTCACTATAG-3'
3'-ATTATGCTGAGTGATATCCACCCGCGTCGAAGCCGACTGCCATGTGG-5'
+1
GMPS, NTPs
T7 RNA Polymerase
5'- -O-P-GGUGGGCGCAGCUUCGGCUGACGGUACACC-3'
N- Spacer- Biotin
100 mM Na_2HPO_4, pH 8
1 mM EDTA
10% DMF
HN NH
$(CH_2)_6$
$(CH_2)_4$
5'
3'

FIGURE 5

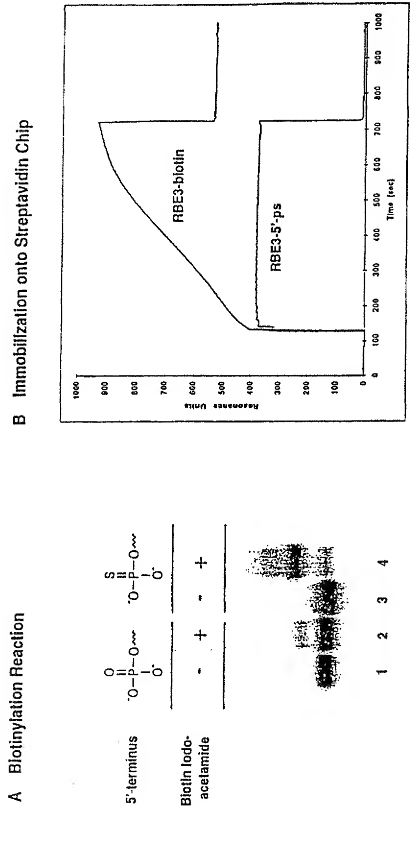
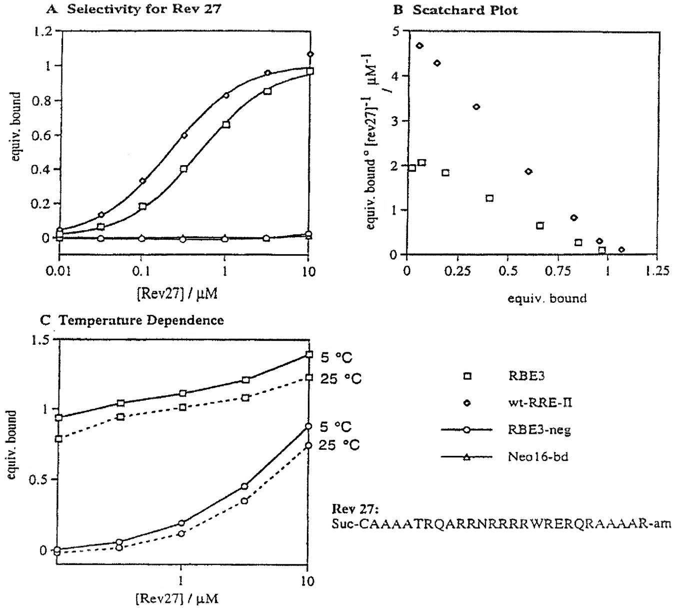

A Biotinylation Reaction
5'-terminus
Biotin Iodo-acetamide
1
2
3
4
B Immobilization onto Streptavidin Chip
RBE3-biotin
RBE3-5'-ps
Resonance Units
Time (sec)

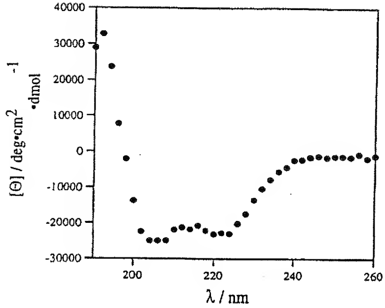
FIGURE 6



Rev 27:
Suc-CAAAATRQARRNRRRRWRERQRAAAAR-am

FIGURE 7

A


40000
30000
20000
10000
0
-10000
-20000
-30000
[Θ] / deg•cm2 •dmol -1
200
220
240
260
λ / nm

B

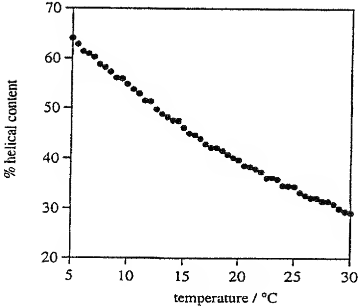

70
60
50
40
30
20
% helical content
5
10
15
20
25
30
temperature / °C

FIGURE 8

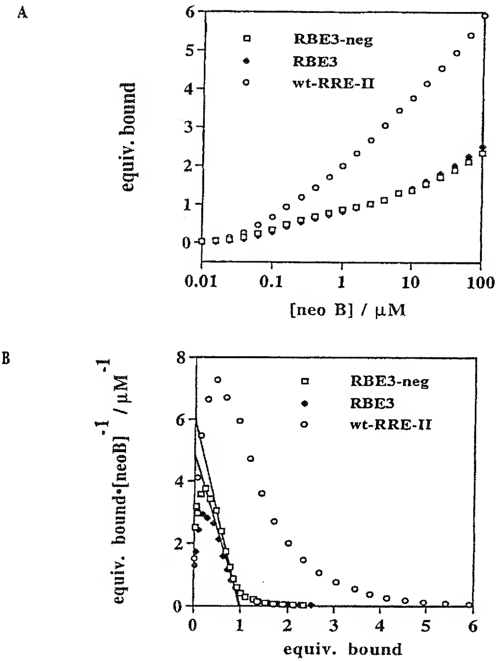
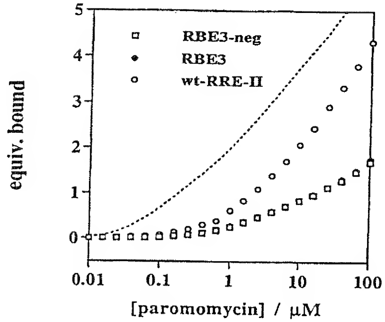

A
6
5
4
3
2
1
0
equiv. bound
RBE3-neg
RBE3
wt-RRE-II
0.01
0.1
1
10
100
[neo B] / μM
B
8
6
4
2
0
equiv. bound•[neoB]-1 / μM-1
RBE3-neg
RBE3
wt-RRE-II
0
1
2
3
4
5
6
equiv. bound

FIGURE 9

A


RBE3-neg
RBE3
wt-RRE-II
equiv. bound
5
4
3
2
1
0
0.01
0.1
1
10
100
[paromomycin] / µM

B

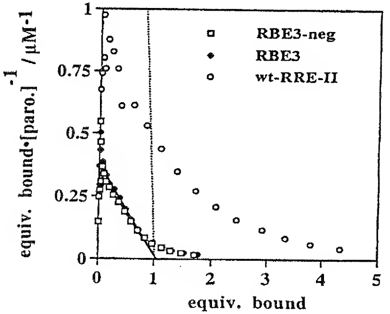

RBE3-neg
RBE3
wt-RRE-II
equiv. bound•[paro.]^-1 / µM-1
1
0.75
0.5
0.25
0
0
1
2
3
4
5
equiv. bound

FIGURE 10

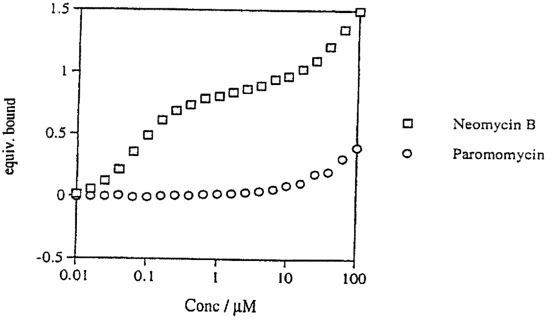
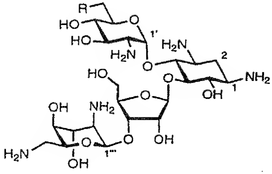
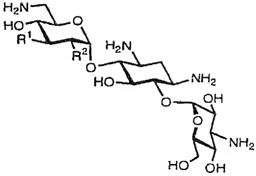

1.5
1
0.5
0
-0.5
equiv. bound
0.01
0.1
1
10
100
Conc / µM
Neomycin B
Paromomycin

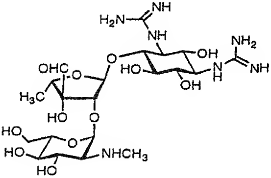
FIGURE 11



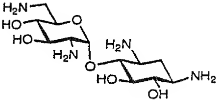
R	
NH_2	Neomycin B
OH	Paromomycin



R^1	R^2	
OH	OH	Kanamycin A
OH	NH_2	Kanamycin B
H	NH_2	Tobramycin



Streptomycin



Neamine

FIGURE 12

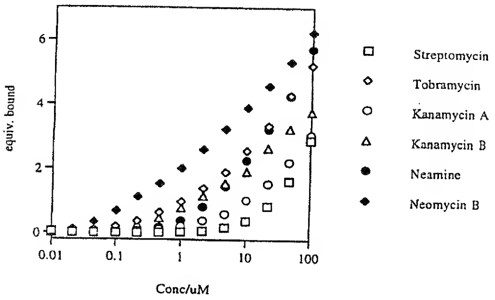

equiv. bound
0
2
4
6
0.01
0.1
1
10
100
Conc/uM
Streptomycin
Tobramycin
Kanamycin A
Kanamycin B
Neamine
Neomycin B

FIGURE 13

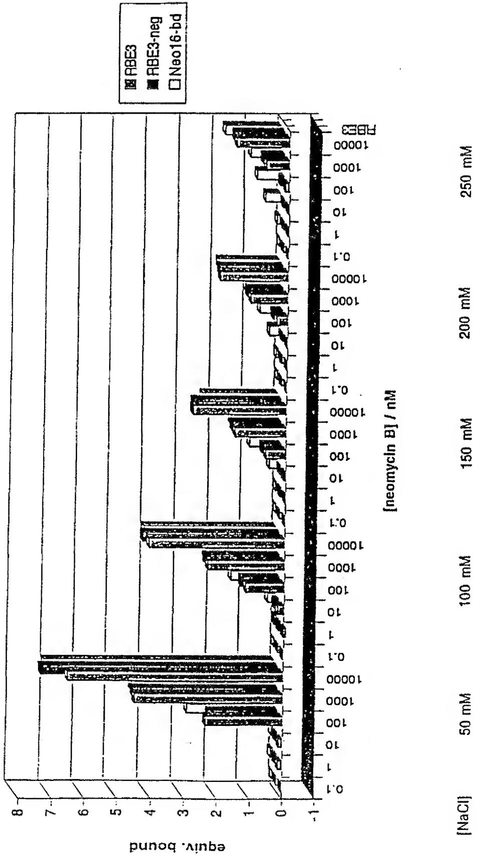

RBE3
RBE3-neg
Neo16-bd
equiv. bound
8
7
6
5
4
3
2
1
0
-1
[neomycin B] / nM
[NaCl]
50 mM
100 mM
150 mM
200 mM
250 mM
0.1
1
10
100
1000
10000
RBE3

FIGURE 14

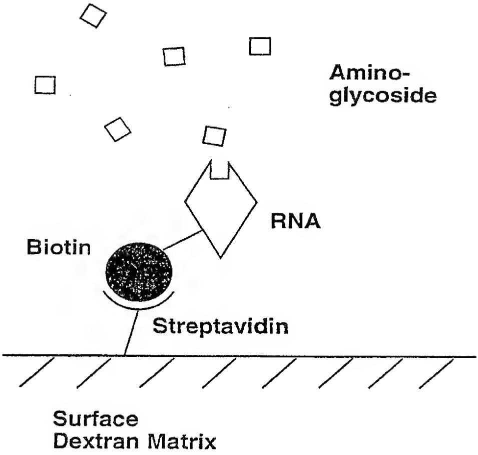

Amino-
glycoside
RNA
Biotin
Streptavidin
Surface
Dextran Matrix

FIGURE 15

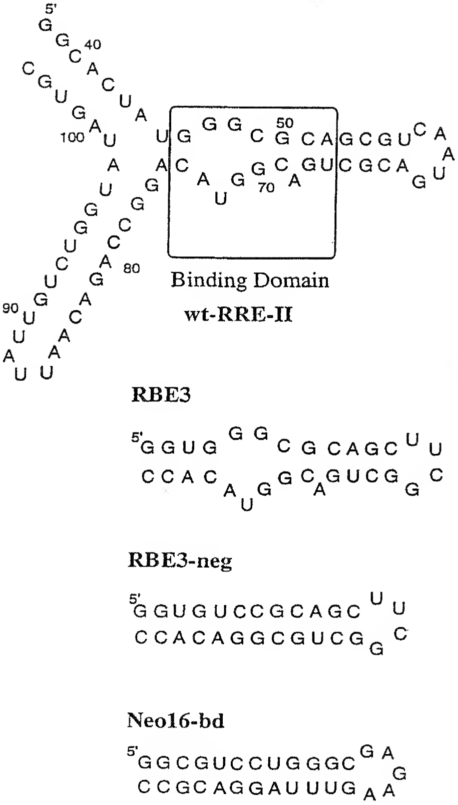
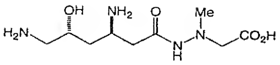
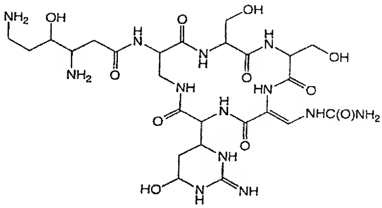

Binding Domain
wt-RRE-II
RBE3
5' G G U G G G C G C A G C U U
C C A C A U G G C A G U C G G C
RBE3-neg
5' G G U G U C C G C A G C U U
C C A C A G G C G U C G G C
Neo16-bd
5' G G C G U C C U G G C G A
G
C C G C A G G A U U U G A A

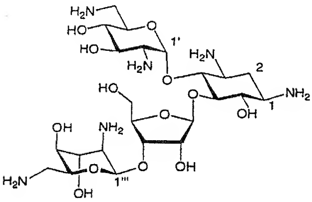
FIGURE 16



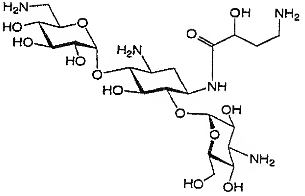
Negamycin



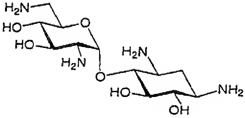
Tuberactinomycin A



Neomycin B

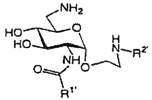


Amikacin

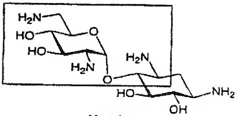


Neamine

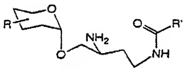
FIGURE 17



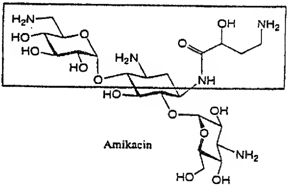
23



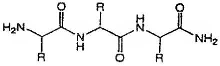
Neamine



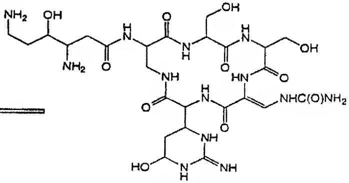
56



Amikacin



33



Tuberacunomycin A

FIGURE 18

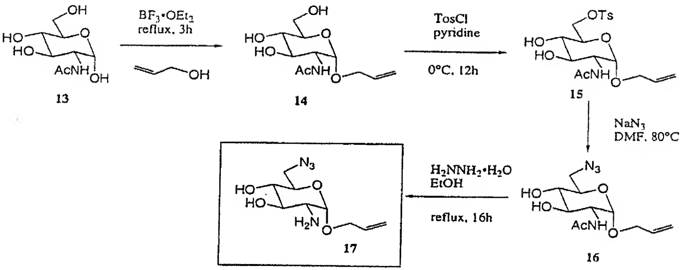
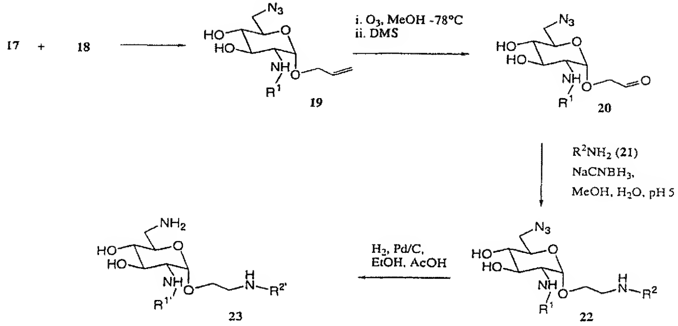

OH
HO
HO
O
AcNH
OH
13
BF3•OEt2
reflux, 3h
OH
OH
HO
HO
O
AcNH
O
14
TosCl
pyridine
0°C, 12h
OTs
HO
HO
O
AcNH
O
15
NaN3
DMF, 80°C
N3
HO
HO
O
AcNH
O
16
H2NNH2•H2O
EtOH
reflux, 16h
N3
HO
HO
O
H2N
O
17

FIGURE 19



R^1	Cbz-Ala, Cbz-Arg(di-Cbz), Cbz-Asn, Cbz-Gln, Cbz-Gly, Cbz-Ile, Cbz-Leu Cbz-Lys(Cbz), Cbz-Phe, Cbz-Pro, Cbz-Thr, Cbz-Val, Cbz
R^2	Bn, propyl, isopropyl, $(CH_2)_2NH_2$, $(CH_2)_3NH_2$, $CH_2CH(NH_2)CH_3$, $(CH_2)_4NH_2$, $(CH_2)_6NH_2$, $(CH_2)_2NHEt$, $(CH_2)_2NH(CH_2)_2NH_2$, $(CH_2)_3NH(CH_2)_3NH_2$, $(CH_2)_3NH(CH_2)_4NH(CH_2)_3NH_2$, $(CH_2)_4NH(CH_2)_3NH_2$, $(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$, $(CH_2)_2N(CH_2CH_2NH_2)_2$, $(CH_2)_2OH$, $(CH_2)_3OH$, $CH(CH_2OH)_2$
$R^{1'}$	Ala, Arg, Asn, Gln, Gly, Ile, Leu, Lys, Phe, Pro, Thr, Val, H
$R^{2'}$	H, propyl, isopropyl, $(CH_2)_2NH_2$, $(CH_2)_3NH_2$, $CH_2CH(NH_2)CH_3$, $(CH_2)_4NH_2$, $(CH_2)_6NH_2$, $(CH_2)_2NHEt$, $(CH_2)_2NH(CH_2)_2NH_2$, $(CH_2)_3NH(CH_2)_3NH_2$, $(CH_2)_3NH(CH_2)_4NH(CH_2)_3NH_2$, $(CH_2)_4NH(CH_2)_3NH_2$, $(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$, $(CH_2)_2N(CH_2CH_2NH_2)_2$, $(CH_2)_2OH$, $(CH_2)_3OH$, $CH(CH_2OH)_2$

FIGURE 20

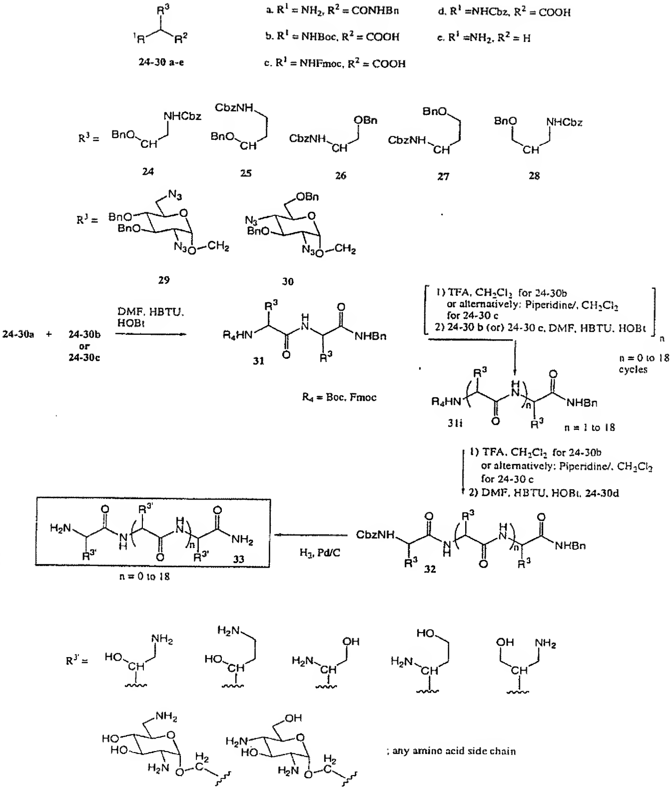
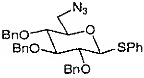
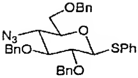

24-30 a-e
a. R1 = NH2, R2 = CONHBn
b. R1 = NHBoc, R2 = COOH
c. R1 = NHFmoc, R2 = COOH
d. R1 =NHCbz, R2 = COOH
e. R1 =NH2, R2 = H
24
25
26
27
28
29
30
DMF, HBTU, HOBt
24-30a + 24-30b or 24-30c
31
R4 = Boc, Fmoc
1) TFA, CH2Cl2 for 24-30b or alternatively: Piperidine/, CH2Cl2 for 24-30 c
2) 24-30 b (or) 24-30 c, DMF, HBTU, HOBt
n = 0 to 18 cycles
31i
n = 1 to 18
1) TFA, CH2Cl2 for 24-30b or alternatively: Piperidine/, CH2Cl2 for 24-30 c
2) DMF, HBTU, HOBt, 24-30d
32
H2, Pd/C
33
n = 0 to 18
; any amino acid side chain

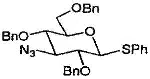
FIGURE 21



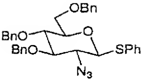
34



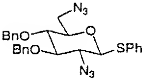
35



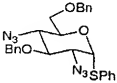
36



37



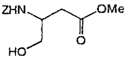
38



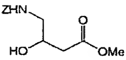
39

FIGURE 22

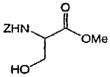
Type I Templates



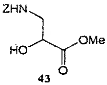
40



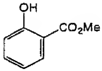
41



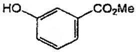
42



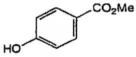
43



44

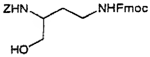


45

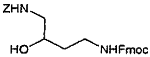


46

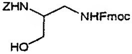
Type II Templates



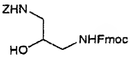
47



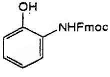
48



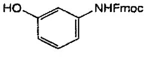
49



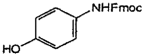
50



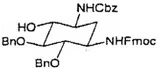
51



52

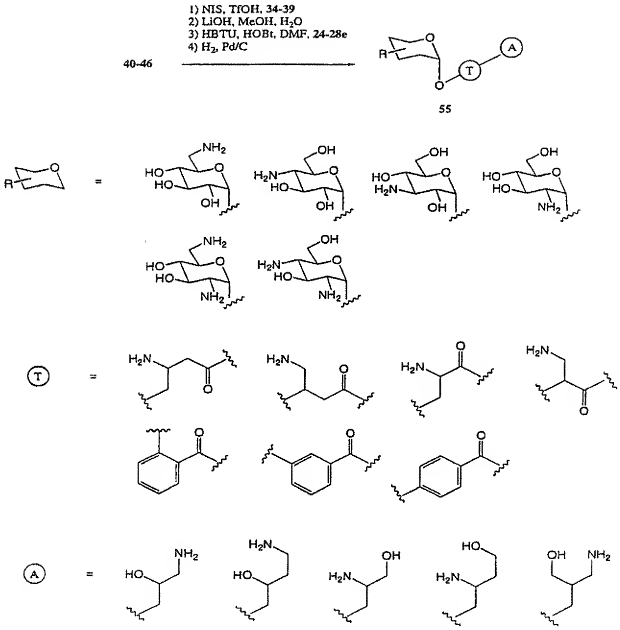


53



54

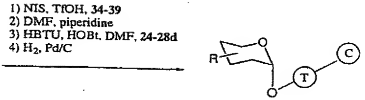
FIGURE 23



1) NIS, TfOH, 34-39
2) LiOH, MeOH, H_2O
3) HBTU, HOBt, DMF, 24-28e
4) H_2, Pd/C
40-46
55

FIGURE 24

47-59



56

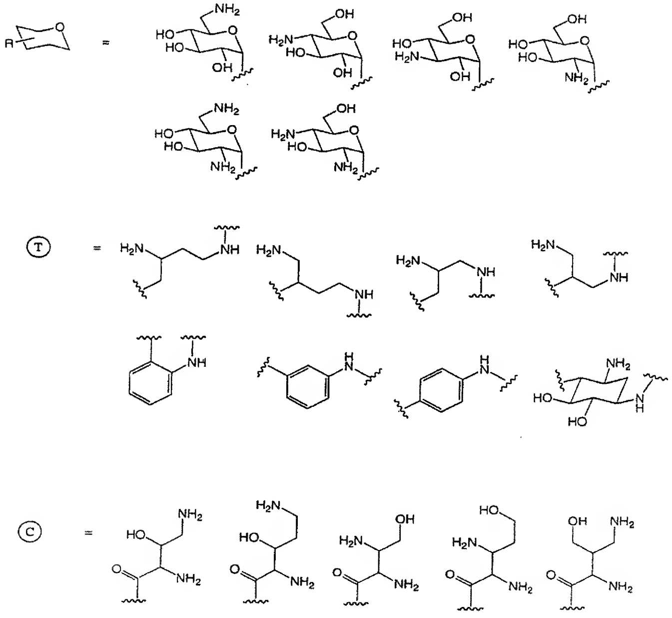
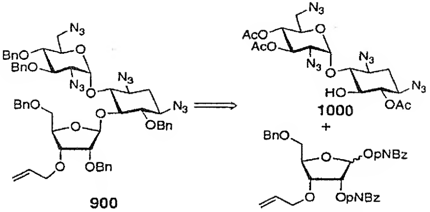


FIGURE 25



900

1000

1100

FIGURE 26

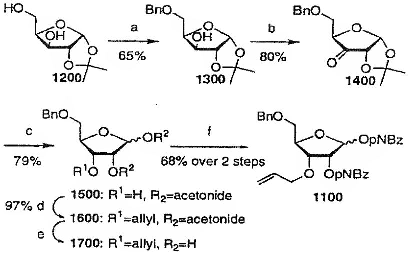
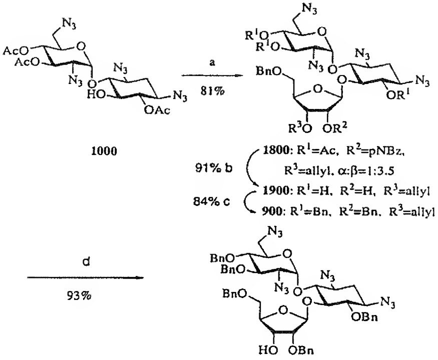

HO
OH
1200
a
65%
BnO
OH
1300
b
80%
BnO
O
1400
c
79%
BnO
OR²
R¹O OR²
f
68% over 2 steps
BnO
OpNBz
OpNBz
1100
1500: R¹=H, R₂=acetonide
97% d
1600: R¹=allyl, R₂=acetonide
e
1700: R¹=allyl, R₂=H

FIGURE 27



1000

2000

FIGURE 28

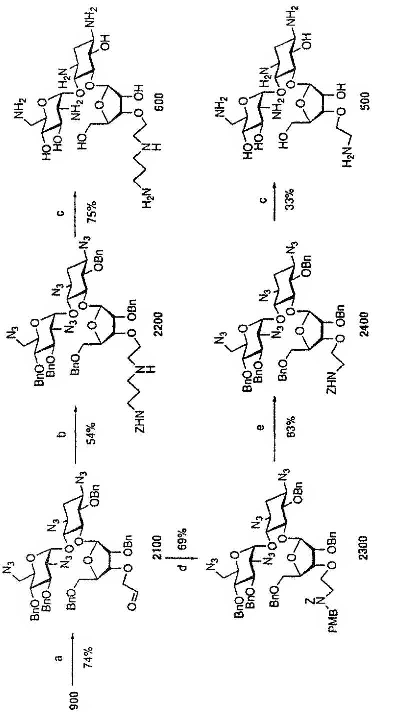
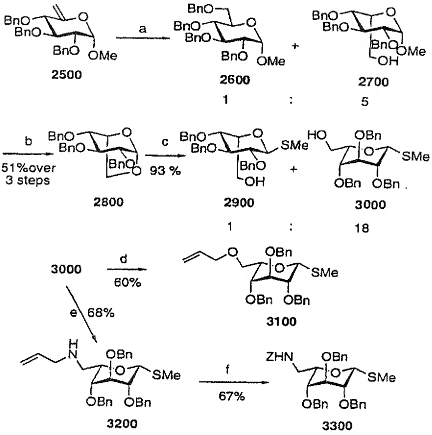


FIGURE 29



BnO
BnO
BnO
OMe
O
2500
a
2600
2700
1 : 5
b
51%over 3 steps
2800
c
93 %
SMe
OH
HO
OBn
2900
3000
1 : 18
3000
d
60%
3100
e 68%
H
N
3200
f
67%
ZHN
3300

FIGURE 30

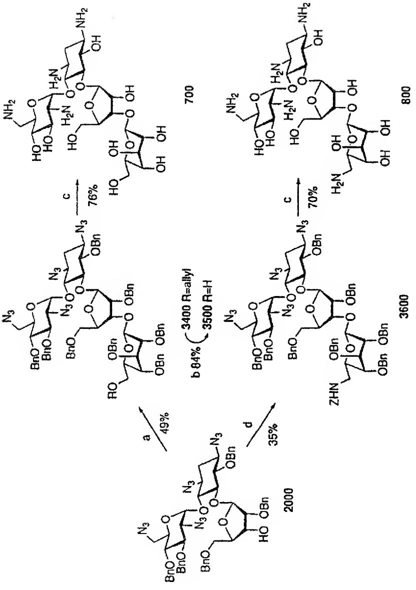
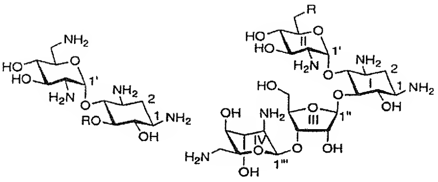


FIGURE 31



100: Neamine; R=H

200: Ribostamycin; R=β-D-ribose

300: Neomycin B : R= NH_2

400: Paromomycin : R=OH

FIGURE 32

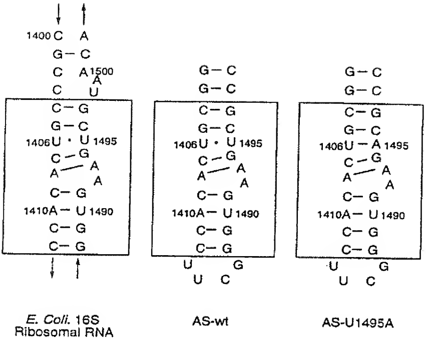

1400 C
A
G – C
C
A 1500
A
C
U
C – G
G – C
1406 U · U 1495
C – G
A – A
A
C – G
1410 A – U 1490
C – G
C – G
E. Coli. 16S Ribosomal RNA
G – C
G – C
C – G
G – C
1406 U · U 1495
C – G
A – A
A
C – G
1410 A – U 1490
C – G
C – G
U G
U C
AS-wt
G – C
G – C
C – G
G – C
1406 U – A 1495
C – G
A – A
A
C – G
1410 A – U 1490
C – G
C – G
U G
U C
AS-U1495A

FIGURE 33

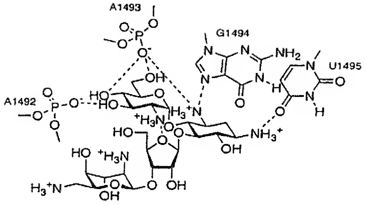


FIGURE 34

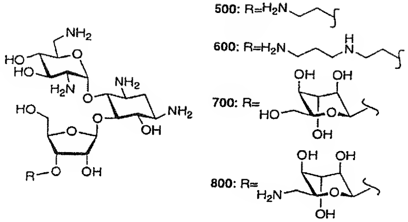
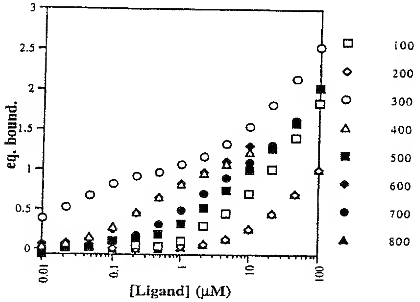

NH2
HO
HO
H2N
O
NH2
NH2
HO
OH
R—O
OH
500: R=H2N
600: R=H2N
H
N
OH OH
700: R=
HO
O
OH
OH OH
800: R=
H2N
O
OH

FIGURE 35



3
2.5
2
1.5
1
0.5
0
eq. bound.
0.01
0.1
1
10
100
[Ligand] (μM)
100
200
300
400
500
600
700
800

FIGURE 36

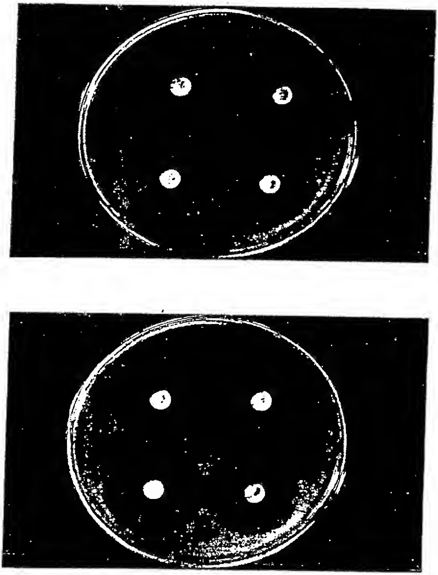


FIGURE 37

Compound	K_d AS wt[a] (μM)	K_d AS U1495A[a] (μM)	Specificity Factor[b]
100	7.8	31	4
200	25	90	4
300	0.019	0.38	20
400	0.20	2.7	14
500	1.7	10	6
600	0.26	1.6	6
700	28	123	4
800	0.70	14	19
Streptomycin	95	74	1

FIGURE 38

A. Diameters of zones of inhibition (DZI), mm[a]				
Antibiotic	Amount	*E. coli*	*S. aureus*	*Ps. aeruginosa*
100	200nmol	18.5	18.5	N.I.
200	33nmol	16.5	14.5	N.I.
300	33nmol	20.5	21.5	9.5
400	33nmol	18	19.5	N.I.
500	33nmol	18.5	18.5	N.I.
600	33nmol	19	21	N.I.
700	33nmol	16.5	11.5	N.I.
800	33nmol	19	19.5	N.I.

B. Minimum inhibitory concentrations (MICs) against *E. coli* ATCC 25922.[b]

Antibiotic	MIC (μM)	MIC (μg/mL)
100	50	26
200	12.5	8
300	1.6	1.5
400	6.25	5.5
500	3.1	2.3
600	1.6	1.4
700	12.5	10
800	3.1	2.6

FIGURE 39

	C1	C2	C3	C4	C5	C6	C1'	C2'	C3'	C4'	C5'	C6'
Neo B	51.4	29.9	49.9	77.3	86.3	74.0	97.0	55.0	69.6	72.1	70.8	41.6
500	51.3	29.5	49.9	76.8	86.2	74.0	97.1	55.0	69.5	72.0	70.9	41.5
600	51.3	29.5	49.9	76.9	86.2	74.0	97.1	55.0	69.5	72.0	70.9	41.5
700	51.3	29.5	49.9	76.9	86.3	73.9	97.0	54.9	69.5	72.0	70.9	41.6
800	51.3	29.5	49.9	76.7	86.3	73.9	97.0	54.9	69.5	72.0	70.9	41.6

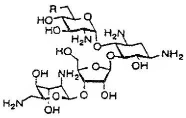
	J (H2ax, H1)	J (H2eq, H1)	J (H2ax, H3)	J (H2eq, H3)
neo B	12.6 Hz	4.1 Hz	12.6 Hz	4.1 Hz
500	12.6 Hz	4.1 Hz	12.6 Hz	4.1 Hz
600	12.6 Hz	4.1 Hz	12.6 Hz	4.1 Hz
700	12.6 Hz	4.1 Hz	12.6 Hz	4.1 Hz
800	12.6 Hz	4.1 Hz	12.6 Hz	4.1 Hz

	J (H2ax, H2eq)	J (H3, H4)	J(H4, H5)	J (H5, H6)
neo B	12.6 Hz	broad	broad	9.4 Hz
500	12.6 Hz	10.5 Hz	10.1 Hz	
600	12.6 Hz	10.4 Hz	9.9 Hz	
700	12.6 Hz	10.3 Hz	10.3 Hz	9.2 Hz
800	12.6 Hz	10.2 Hz	10.2 Hz	9.3 Hz

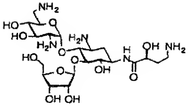
	J (H1, H6)	J (H1', H2')	J (H2', H3')	J (H3', H4')
neo B	10.4 Hz	4.0 Hz	10.8 Hz	9.2 Hz
500	10.7 Hz	4.0 Hz	10.8 Hz	9.3 Hz
600	10.6 Hz	3.9 Hz	10.9 Hz	9.5 Hz
700	10.6 Hz	4.0 Hz		9.4 Hz
800	10.4 Hz	4.0 Hz	10.9 Hz	9.3 Hz

	J (H4', H5')	J (H5', H6'a)	J (H6'a, H6'b)
neo B		6.7 Hz	13.6 Hz
500	9.3 Hz	6.4 Hz	13.6 Hz
600	9.5 Hz	6.4 Hz	13.2 Hz
700	9.4 Hz	6.3 Hz	13.7 Hz
800	9.3 Hz	6.4 Hz	13.7 Hz

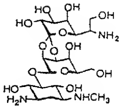
FIGURE 40



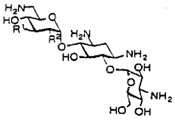
R	
NH_2	Neomycin B
OH	Paromomycin



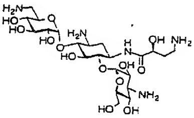
Butirosin B



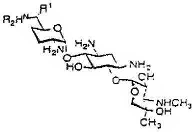
Hygromycin B



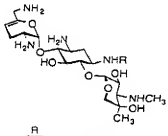
R^1	R^2	
OH	OH	Kanamycin A
OH	NH_2	Kanamycin B
H	NH_2	Tobramycin



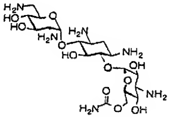
Amikacin



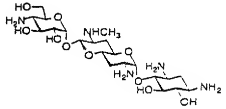
R^1	R^2	
CH_3	CH_3	Gentamicin C_1
CH_3	H	Gentamicin C_2
H	H	Gentamicin C_{1a}



R	
H	Sisomicin
CH_2CH_3	Netilmicin



Nebramycin factor 4

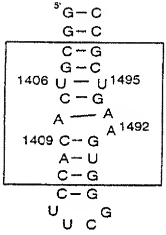


Apramycin

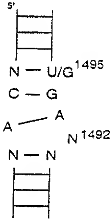
FIGURE 41

Compound	Footprints [a]	Resistance	Organism
Hygromycin B	G1494 (s) A1408 (e)	U1495C	*Tetrahymena*
Neomycin B Paromomycin Kanamycins Gentamycins	G1494 (s) A1408 (s) G1491 (w) C525 (e)	G1491C [c] G1491A [d] C1409G [d] ^{7m}G1405 [e] ^{1m}A1408 [f]	*E. coli* *Tetrahymena* *Yeast mitochondria* *Microm.purp.* *Strept. tenjim.*
Neamine Apramycin	G1494 (s) A1408 (s) G1491 (w)	^{1m}A1408 [f]	*Strept. tenjim.*
Ribostamycin		^{1m}A1408 [f]	*Strept. tenjim.*

FIGURE 42



AS-wt



Sequence Requirements
for Paromomycin Recognition

FIGURE 43

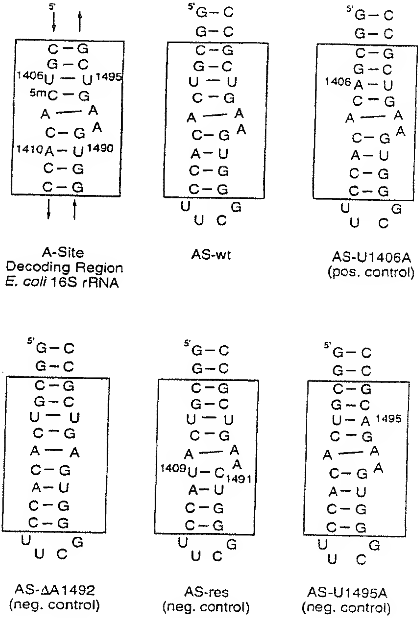
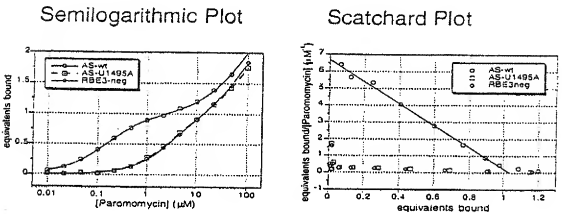

5'
1406
1495
5m
1410
1490
A-Site
Decoding Region
E. coli 16S rRNA
AS-wt
AS-U1406A
(pos. control)
AS-ΔA1492
(neg. control)
AS-res
(neg. control)
1409
1491
AS-U1495A
(neg. control)

FIGURE 44



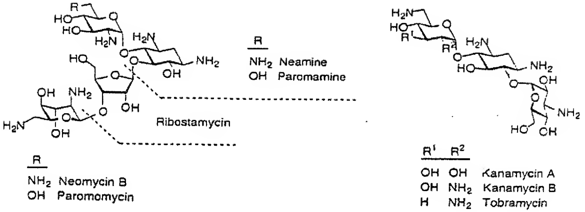
Sequence	K_d (μM)
AS-wt	0.15
AS-U1495A	2.83
RBE3-neg	3.19

FIGURE 45

Compound	AS-wt	U1406A	U1495A	AS-res	ΔA1492
Neomycin B	0.019	<0.01	0.38	0.48	0.32
Ribostamycin-3''-R[1]	0.26	0.075	1.6	0.89	0.58
Paromomycin	0.20	0.027	2.7	5.7	5.7
2'''-OH-Neomycin B	0.70	0.090	14	7.3	6.2
Ribostamycin-3''-R[2]	1.7	0.17	10	6.7	5.1
Kanamycin B	1.4	4.4	4.0	3.5	2.7
Tobramycin	1.5	2.1	4.1	7.9	4.5
Gentamycin	1.7	9.9	12	18	16
Apramycin	6.3	9.3	13		
2''',6'''-di-(OH)-Neo. B	28	4.9	>100	>100	>100
Ribostamycin	25	11	90	52	38
Kanamycin A	18	28	33	37	32
Neamine	7.8	5.5	31		
Butirosin	27	1.8	99		
Paromamine	>100	>100	>100	>100	>100
Hygromycin B	>100	>100	>100	>100	>100
Streptomycin	94	66	74		

$R^1 = (CH_2)_2NH(CH_2)_3NH_2$ $R^2 = (CH_2)_2NH_2$

FIGURE 46



(structures of other aminoglycosides in Figure 1)

FIGURE 47

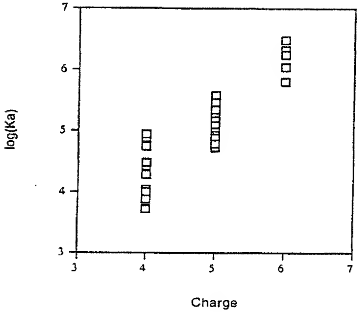


FIGURE 48

Compound	AS-wt	U1495A	Specificity *vs.* U1495A
Paromomycin			
HBS-buffer alone	0.20	2.7	14
+ 50 mM NH_4Cl	0.29	6.5	23
+ 150 mM NH_4Cl	1.1	32	28
pH 7.8	0.53	7,7	15
Neomycin B			
HBS-buffer alone	0.019	0.38	20
+ 50 mM NH_4Cl	0.025	1.1	43
+ 150 mM NH_4Cl	0.15	6.7	43
pH 7.8	0.044	0.91	21

FIGURE 49

Compound	Average K_d(nonspec.) (μM)	Specificity *vs.* AS-wt	Specificity *vs.* U1406A
4,5-linked			
Neomycin B	0.39	20	>40
Paromomycin	4.7	20	200
2'''-OH-Neomycin B	9.0	10	100
2''',6'''-di-(OH)-Neo. B	150	5	30
Ribostamycin-3''-R^2	7.4	4	40
Ribostamycin-3''-R^1	1.0	4	10
Butirosin	99	4	60
Neamine	31	4	6
Ribostamycin	60	2	5
4,6-linked			
Gentamycin	16	9	2
Tobramycin	5.5	4	3
Kanamycin B	3.4	2	<1
Apramycin	13	2	1
Kanamycin A	34	2	1
Control			
Streptomycin	74	<1	1

$R^1 = (CH_2)_2NH(CH_2)_3NH_2$

$R^2 = (CH_2)_2NH_2$

FIGURE 50

Compound	Neo16-bd	AS-wt	RBE3	RBE3-neg	wt-RRE-II
Neomycin B	<0.01	0.019	0.24	0.16	0.25
Ribostamycin-3"-R[1]	<0.01	0.26	0.38	0.56	0.31
Paromomycin	0.19	0.20	2.3	2.8	2.8
2'''-OH-Neomycin B	<0.01	0.70	3.1	3.5	7.8
Ribostamycin-3"-R[2]	<0.01	1.7	1.7	5.2	2.7
Kanamycin B	0.09	1.4	1.2	0.80	0.51
Tobramycin	0.39	1.5	0.38	0.16	0.41
2''',6'''-di-(OH)-Neo. B	0.08	28	36	150	57
Ribostamycin	0.09	25	15	26	25
Kanamycin A	2.1	18	8.3	14	5.9
Streptomycin	>100	94	100	nd	80

$R^1 = (CH_2)_2NH(CH_2)_3NH_2$ $R^2 = (CH_2)_2NH_2$

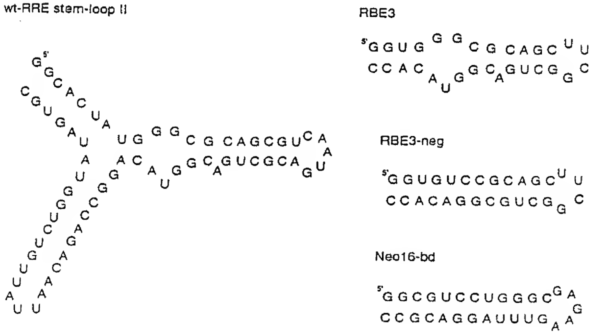
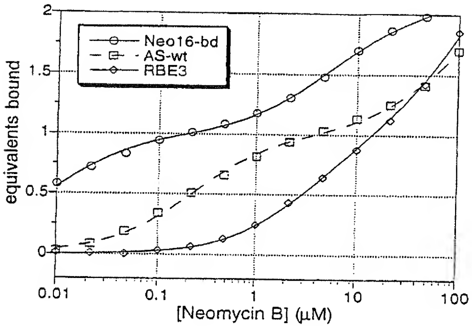


FIGURE 51

Compound / temperature (°C)	AS-wt	Neo16bd	RBE3
Paromomycin			
500	0.058	0.059	1.4
1500	0.10	0.11	1.7
2500	0.18	0.19	2.4
3500	0.45	0.32	3.0
Neomycin B [a]			
500	0.11	<0.01	2.2
1500	0.17	<0.01	2.9
2500	0.22	<0.01	3.2

[a] conditions: HBS-buffer + 150 mM NH_4Cl.

FIGURE 52



Sequence	K_d (μM)
Neo16bd	<0.01
AS-wt	0.22
RBE3	3.22

FIGURE 53

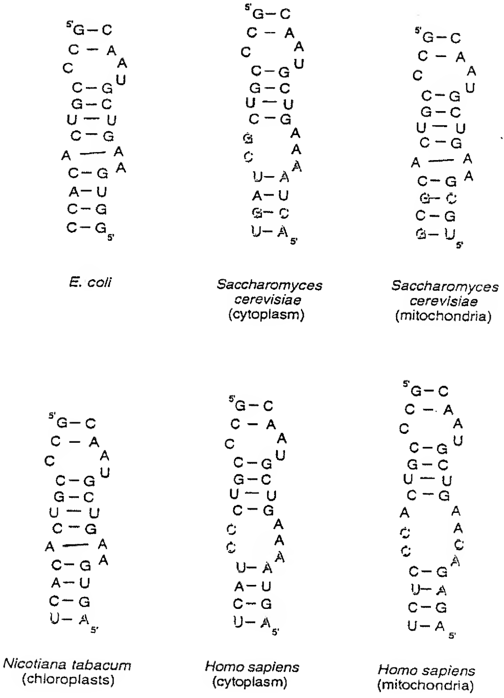
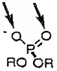
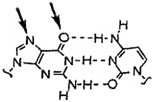

E. coli
Saccharomyces cerevisiae (cytoplasm)
Saccharomyces cerevisiae (mitochondria)
Nicotiana tabacum (chloroplasts)
Homo sapiens (cytoplasm)
Homo sapiens (mitochondria)

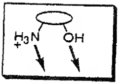
FIGURE 54



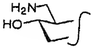
Phosphates



GC Base Pair



Hydroxyamines

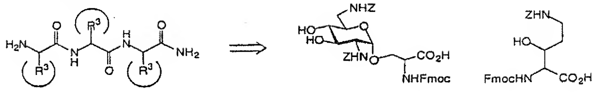


1,3-

1,2-

FIGURE 55

A. Peptidic Library



B. Carbohydrate Library

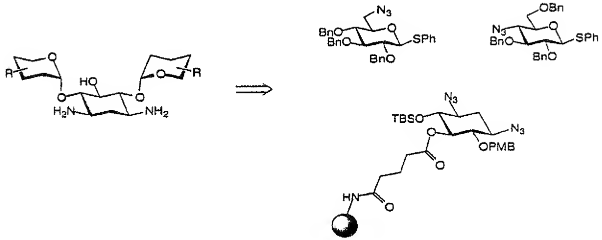


FIGURE 56

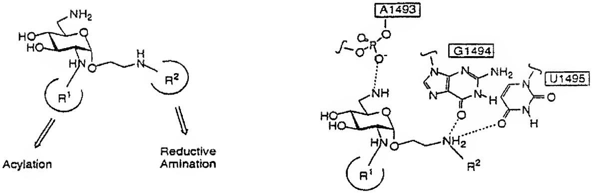
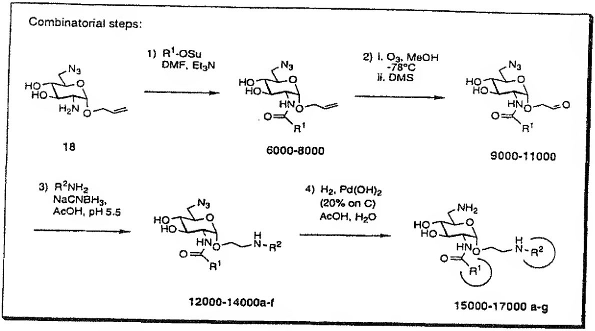

NH2
HO
HO
HN
H
N
R2
R1
Acylation
Reductive
Amination
A1493
G1494
U1495
NH
NH2
O
R2

FIGURE 57


Combinatorial steps:
1) R^1-OSu DMF, Et_3N
2) i. O_3, MeOH -78°C ii. DMS
3) R^2NH_2 $NaCNBH_3$, AcOH, pH 5.5
4) H_2, $Pd(OH)_2$ (20% on C) AcOH, H_2O
18
6000-8000
9000-11000
12000-14000a-f
15000-17000 a-g

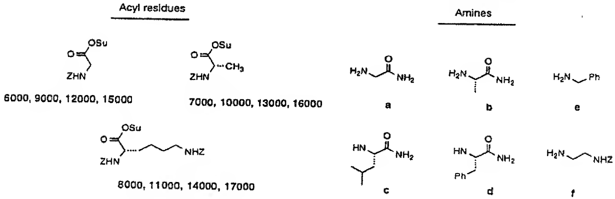
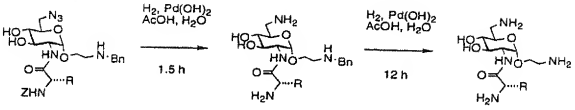

Acyl residues
Amines
6000, 9000, 12000, 15000
7000, 10000, 13000, 16000
8000, 11000, 14000, 17000
a
b
e
c
d
f

FIGURE 58



12000-14000e 15000-17000 e 15000-17000g

FIGURE 59

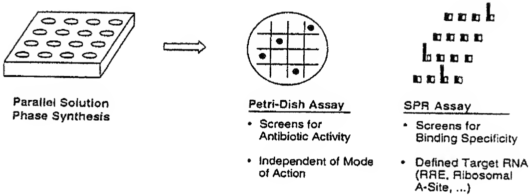

Parallel Solution
Phase Synthesis
Petri-Dish Assay
• Screens for Antibiotic Activity
• Independent of Mode of Action
SPR Assay
• Screens for Binding Specificity
• Defined Target RNA (RRE, Ribosomal A-Site, ...)

FIGURE 60

	R^1CO	R^2NH	AS-wt	U1406A	U1495A	AS-res	ΔA1492
15000a	Gly	$GlyNH_2$	110	81	95	140	120
15000b		$AlaNH_2$	140	110	120	430	270
15000c		$ValNH_2$	310	250	270	>500	>500
15000d		$PheNH_2$	60	43	71	120	100
15000g		NH_2	79	86	110	96	81
15000h		$NH(CH_2)_2NH_2$	38	38	39	64	46
16000a	Ala	$GlyNH_2$	34	25	27	54	37
16000b		$AlaNH_2$	480	320	350	>500	>500
16000c		$ValNH_2$	>500	>500	>500	>500	>500
16000d		$PheNH_2$	170	150	150	180	130
16000g		NH_2	120	100	100	130	130
16000f		$NH(CH_2)_2NH_2$	59	57	57	83	56
17000a	Lys	$GlyNH_2$	26	31	34	43	62
17000b		$AlaNH_2$	66	48	55	150	92
17000c		$ValNH_2$	180	150	140	370	300
17000d		$PheNH_2$	290	260	240	350	360
17000g		NH_2	16	13	14	34	19
17000f		$NH(CH_2)_2NH_2$	19	18	17	51	30

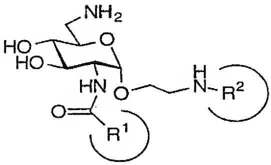


FIGURE 61

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/00549

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C07H 1/00, 15/04, 15/12
US CL : 530/322; 536/1.11, 4.1, 13.2, 22.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/322; 536/1.11, 4.1, 13.2, 22.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, STN ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	HENDRIX, M. et al.Hydroxyamines as a New Motif for the Molecular Recognition of Phosphodiesters: Implications for Aminoglycoside-RNA Interactions, Angew. Chem. Int. Ed. Engl., 1997, 36, No. 1/2, pages 95-98	1,10
A,P	Rodriguez, E.C. et al. A Strategy for the Chemoselective Synthesis of O-Linked Glycopeptides with Native Sugar-Peptide Linkages. J. Amer. Chem. Society, 1997, 119, pages 9905-9906.	1,10

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 MARCH 1998	08 APR 1998

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	MICHAEL BORIN
Facsimile No. (703) 305-3230	Telephone No. (703) 305-4506

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/00549

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1,10

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1,10, drawn to a compound, as defined in the claim 1, and the corresponding library of compounds.
Group II, claims 2,11, drawn to a compound, as defined in the claim 2, and the corresponding library of compounds.
Group III, claims 3, 12, drawn to a compound, as defined in the claim 3, and the corresponding library of compounds.
Group IV, claims 4,13, drawn to a compound, as defined in the claim 4, and the corresponding library of compounds.
Group V, claims 5, 14, drawn to a compound, as defined in the claim 5, and the corresponding library of compounds.
Group VI, claims 6-9, drawn to compounds of the general formula defined in claim 6.
Group VII, claims 15, 16 drawn to a sensorchip having immobilized RNA.
Group VIII claims 17 (generic claim), 18, drawn to a sensorchip having immobilized RNA and a hydroxylamine substructure attached to the said RNA, the said hydroxylamine structure being the compound of Group I.
Group IX, claims 17 (generic claim), 19, drawn to a sensorchip having immobilized RNA and a hydroxylamine substructure attached to the said RNA, the said hydroxylamine structure being the compound of Group II.
Group X, claims 17 (generic claim), 20, drawn to a sensorchip having immobilized RNA and a hydroxylamine substructure attached to the said RNA, the said hydroxylamine structure being the compound of Group III.
Group XI, claims 17 (generic claim), 21, drawn to a sensorchip having immobilized RNA and a hydroxylamine substructure attached to the said RNA, the said hydroxylamine structure being the compound of Group IV.
Group XII, claims 17 (generic claim), 22, drawn to a sensorchip having immobilized RNA and a hydroxylamine substructure attached to the said RNA, the said hydroxylamine structure being the compound of Group V.
Group XIII, drawn to method of detection of binding a compound to RNA.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The products of Groups I to VI encompass different scope of different compounds which do not share a common technical feature. For example, product of Group I as compared to the product of Group II is i) limited to one glycoside structure, whereas this glycoside structure is one of many distinct moieties encompassed by radical R3 in the compound of Group II; ii) comprises one glycoside moiety as opposed to two moieties in the product of Group II; iii) does not encompass polypeptide compounds of the Group II. Other numerous patentably distinct differences exist between the products of Groups I-VI. Further, for example, the product of Group VII is limited to a product (sensorchip) having immobilized RNA only as opposed to products of the Groups VIII-XII containing a hydroxylamine substructure in addition to the said RNA. Groups VIII - XII are different for the same reasons as Groups I-VI. Group XIII is an independent method of use.